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The Journal of Pediatrics

VOL. 4 MARCH, 1934 NO. 3

Original Communications

OBESITY IN CHILDREN

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LOS ANGELES, CALIF.

THE undernourished child has so usurped the attention and worries of the modern mother that his counterpart, the overweight child, usually is ignored unless, perchance, he is held up as an object of envy to that perennial pediatric problem, the child who won't eat. The average physician gives little thought to obesity. If he gives any advice at all to the parents of a fat child, it usually consists of certain admonitions in a very professorial manner and, perhaps, a list of foods or even a diet list. Consequently pediatric literature contains little concerning the subject even though it is one of extreme importance to the internist and of tremendous interest to the laity. Some years ago DuBois said, "We do not know why certain persons grow fat; perhaps it would be more accurate to say that we do not know why all individuals in this overnourished country do not grow fat." There still are many unknown factors in the pathogenesis of obesity in children.

It is difficult to determine what actually constitutes obesity in a child. So much emphasis is placed on the various height-weight tables that individual differences in body build and in constitutional make-up often are overlooked. It is stated generally that a child is obese when the excess surpasses 20 per cent. While this holds for the majority, one must keep in mind the occasional young "husky" of splendid build and muscular development, who may exceed that limit over the average, and yet not be obese. In the minds of the laity and, indeed, even among pediatricians, there exists considerable confusion over this question of when a child is overweight. Just as there is no general rule that will sharply distinguish undernutrition and normal nutrition, so there is the same lack of definite standards which separate overnutrition or obesity from normal nutrition. Children often

Presented before meeting of the staff of Children's Hospital, Los Angeles, 1933.

are considered well nourished or perhaps pleasingly plump by their parents or family physician, and yet may be obviously obese to the casual observer.

A brief review of fat metabolism in normal individuals may be helpful in evaluating some of the chemical and metabolic studies on obesity. The fats consist of a combination of fatty acids and glycerin, the triglycerides of palmitic, stearic and oleic acid. To be absorbed from the intestinal tract, fats first must be saponified by the action of the pancreatic juice, resulting in a separation of the fatty acids from the glycerin. After passage through the intestinal wall, these split portions are reunited, but in a different form, so as to resemble the natural fat of the individual. The fats are carried to the blood stream through an indirect route by means of the lacteals and the thoracic duct. The destination of the blood fat is twofold—the fat depots including the retroperitoneal and subcutaneous tissues where it is stored, and the liver where it undergoes certain chemical changes which allow for subsequent use as fuel.

It has been proved that carbohydrates are capable of producing fats directly, but a direct fat production from protein is not certain although the latter can be split into a carbohydrate which may lead to fat formation. Stored fat represents approximately one-sixth of one's body weight. During starvation most of the energy requirement of the body comes from the utilization of this stored fat, which is carried by the blood stream to the liver and there metabolized. When the diet contains ample carbohydrate and protein, little of the fat intake is burned, most of it being stored. The statement, "fats burn only in the fire of carbohydrate," is one of the few facts of physiology which the medical student rarely forgets. For the combustion of two molecules of fatty acid, one molecule of dextrose is necessary.

The make-up of the diet is important for body growth and maintenance, supply of energy involved in muscular work, and the production of body heat. Fat is not absolutely necessary in the diet for, as a source of energy, it may be replaced by carbohydrate or protein. The protein requirements in infancy and childhood necessary for the maintenance of life and the building of body tissue vary from 2 to 4 grams per kilogram of body weight. The energy for work and heat production results from the oxidation within the body of the carbon and hydrogen of fats, carbohydrates, and amino acids. If the energy used is less than is supplied by the food, the body usually gains weight due to fat storage; if the energy output is greater than the food supplies, the body loses weight due to the utilization of the available storehouses.

However, the caloric intake and energy expense do not always account for the weight curve of human beings. Neuman[2] in 1902 experimented on himself for a steady period of two years during which

time he maintained his normal weight and well-being on diets equivalent to 1,750, 2,200, and 2,400 calories. Grafe and Koch[3] studied a fourteen-year-old boy weighing 26.5 kilograms (140 centimeters in height) who was given diets consisting of 88 calories and 51 calories per kilogram of body weight for approximately two weeks each without any change in his weight curve. When the diet was further reduced to 40 calories per kilogram, less than half of the original diet of 88 calories, the boy lost only 0.5 kilogram during another two-week period.

Numerous other experiments have been reported demonstrating the constancy with which most children, just as most adults, maintain their normal weight and growth curves despite the fact that the food intake fluctuates, and their physical activity varies from day to day. When a child loses weight as a result of illness, he quickly regains that loss when he begins to eat again and reaches approximately the same basic weight as before. This weight equilibrium is dependent upon a sensitive mechanism of regulation, the disturbance of which causes some children to be fat and others to be lean.

Barker[4] pointed out that the term "obesity" is derived from the Latin word *obesus* meaning "that has eaten itself fat, stout, plump," which derivation suggests that for those who first introduced it in the seventeenth century the word designated a condition actually dependent on eating too much. Today there are many who still believe that there is only one basic cause of obesity—overeating. The common practice, however, is to divide obese individuals into two groups: the exogenous as exemplified by the commonly cited Falstaff; and the endogenous type, as represented by the fat boy of Dickens' *Pickwick Papers*.

Newburgh[5] and the champions of exogenous obesity argued that in obese patients the energy expended is less than the caloric intake, such laziness and gluttony resulting in a positive energy balance. They further pointed out that if the potential energy intake be reduced below the output, the obese patient will lose weight. But Silver and Bauer[6] were not convinced by this interpretation, which does not explain why the obese child actually consumes more food than is required to maintain his normal weight or why his energy output is usually decreased.

Obviously, there is some inherent tendency, be it constitutional, metabolic, endocrine or neural in origin, which must be offered in explanation of why children of the same family, living in the same environment, and eating the same food will differ in this fat regulating mechanism. Recently I have been observing very interesting twins, four years of age, one of whom (the boy) is of normal weight, height, and development, while his sister, when first examined, weighed 61½ pounds, being 26 pounds heavier than her twin brother

and correspondingly larger in body build. In this family there is a definite tendency to obesity, particularly on the mother's side. Bauer[6] reports a familial incidence of obesity in some 88 per cent of his cases, and emphasizes the constitutional make-up of the individual, stressing the etiologic importance of the congenital and hereditary nature of the obese state. Von Noorden[7] found 70 per cent of his obese patients came from families in which obesity prevailed. In approximately 75 per cent of the obese children we have been studying, there is a definite family history of obesity.

Various races and tribes tend to be either fat or thin, and breeders of live stock can testify that certain breeds cannot be fattened even though they are fed and treated the same as those which are made to gain weight rapidly. Danforth[8] of Stanford reported a strain of yellow mice with a definite tendency to obesity at maturity. Females were more often affected than males, and the excess weight often was three times as great as that of normal adults of other strains. On starvation diets, these fat mice could be reduced easily. Danforth pointed out the interesting observation that this strain of yellow mice had fewer litters and that the period of fecundity was much shorter than the average for other strains.

Various disorders of metabolism, both qualitative and quantitative, have been suggested in an attempt to explain obesity. The theory of a qualitative abnormality is chiefly of German origin. Von Bergmann of Berlin introduced the terms "lipophilia" and "lipomatosis." A probable localized and independent disposition of certain tissues to obesity is illustrated by reported cases[10] of autogenous grafts transplanted from the abdominal wall to the back of the hand. In these instances definite unilateral obesity has been observed, demarcated by the limits of the skin graft on the dorsum of the hand which rarely becomes fat. The lipophilia or tendency to accumulate fat of the transplanted abdominal wall apparently is retained even though severed from the original blood and nerve supply.

Wang, Strouse, and Saunders[11] demonstrated that on a high fat diet, the respiratory quotient, or the ratio between the volume of carbon dioxide expired and the volume of oxygen inspired in a given time, was constantly higher in obese subjects, suggesting that in obesity, fat is less easily oxidized or deposited more readily. This result may be explained equally well, as Wilder[12] suggested, on the theory that the larger stores of glycogen, undoubtedly present in the overweight individual, are utilized when the carbohydrate intake is low. Both processes, sugar burning and fat storage, raise the respiratory quotient.

Some have wondered if obesity is a qualitative anomaly of metabolism more or less analogous to diabetes mellitus. Obesity frequently

accompanies or is a precursor of both mild and severe cases of diabetes and may therefore be due to increased transformation of carbohydrate into fat.

The theories of a quantitative disorder in the metabolism of the obese individual are based on a marked reduction in the expenditure of energy. Von Noorden[7] first observed that the obese subject produces less than the normal heat when calculated on the basis of kilograms of weight. But Rubner[13] in his experiment on two brothers, one fat and the other thin, demonstrated that the basal metabolism per square meter of body surface is the same in the two types of individual. Grafe and Graham[14] in a well controlled experiment observed a 40 per cent increase in the basal metabolic rate without gain in weight in a dog fed twice the minimum requirement during a fifty-nine-day period. Grafe assumed that amounts of food over the actual need of the normal individual tend to increase metabolism sufficiently to burn up the excess. Therefore, the failure of the obese individual to respond normally to this stimulus is the reason for his obesity, according to Grafe's theory.

Strang and Evans[15] have emphasized recently that the basal metabolism in obesity is even increased rather than decreased if the probable mass of muscle or active tissue is made the basis for calculating the energy metabolism rather than the patient's actual weight. This is borne out in Bauer's[16] notation that Heinbecker found a distinct increase in the basal metabolism of Eskimos, who are characteristically obese. Strouse[17] and his coworkers have stated that no consistent relation exists between constitutional obesity and basal metabolism. They conclude that "neither excessive undernutrition nor excessive overweight is associated with a constant change in basal metabolism."

Topper and Mulier[18] working with seventy overweight, but otherwise normal, children concluded that the basal metabolism is usually normal in obese children with a tendency toward a high normal rate. They found an apparent association between the prepuberty period and an increased basal rate due, perhaps, to the increase in growth, increased activity of the endocrine glands, and the awakening of sexual life. These investigators used the Pirquet and Talbot standards and did not take into consideration the patient's body weight. Dr. Howard West's determinations of the basal metabolic rate in a considerable number of our obese patients were not conclusive except to agree with Anne Topper and others that the basal rate in obese children is usually within normal limits, even approaching a high normal in many instances. Relatively few had rates below minus ten, which is considered the lower limit of normal. One encounters many difficulties in obtaining a correct basal rate in most children with the apparatus and methods used in office practice. The child's hunger, his apprehension and frequent behavior difficulties require much time, effort, and

patience to overcome. With the small portable machine, accurate determinations of the basal metabolic rate are not obtainable in the average child under nine or ten years of age. The metabolic chamber seems indispensable in careful studies of basal metabolism, but its extensive equipment and the necessity for trained personnel precludes its use in most hospitals and clinics.

Plaut[19] in 1922 reported a very definite lowering of the specific dynamic action of food in obese individuals and a very marked rise in those persons with so-called constitutional thinness. By specific dynamic action of a foodstuff is meant the increase in the heat production of the organism following the ingestion of that foodstuff. Wang, Strouse and Saunders[11] demonstrated that protein showed a very slight specific dynamic action in obese people while normal persons and those extremely thin showed a very high specific dynamic action of protein. No significant changes from the normal were observed with the specific dynamic action of carbohydrate and fat. However, this lessening of the specific dynamic action of protein probably would have a relatively small effect on the total metabolism of the fat child and can hardly be considered a primary cause of obesity.

Considering the theories on the rôle of hormones in the regulation of body weight, we also find confusion. Englebach,[20] for instance, classified every case of endogenous obesity in children on the basis of clinical characteristics, often not clear-cut, and from inference, grouped them under thyrogenic, pituitary and other types. These endocrine groups, however, are not definite and are subject to much speculation.

Those obesities of infancy and childhood attributed to diminished thyroid activity are less common than those due to the supposed involvement of the pituitary alone, or in conjunction with thyroid deficiency. The obesities of infants and young children are more apt to be thyrogenous in origin, in contrast to the more commonly assumed pituitary origin of obesities in older children and adolescents. The retardation of growth, delayed appearance of the epiphyses, delayed dentition, lack of normal mental development, the pale, dry and coarse skin and other characteristics of cretinism are too well known to warrant more than mentioning. Juvenile hypothyroidism and myxedema are similar to the adult picture.

Obesity of older children associated with infantile genitals has been considered to be due to alterations of the hypophysis. Fröhlich's syndrome or adiposogenital dystrophy is characterized clinically by a distribution of fat with the lower abdomen, hips, and thighs chiefly involved. Enlargement of the breasts is often pronounced. Widely separated upper incisors are said to be characteristic although they do not occur in all cases, and the condition may be present in persons with no signs of hypopituitarism. The genitals are strikingly small and undeveloped, so much so that sometimes they are buried

in the fatty tissues around them. Many transitory stages exist between the Frölich type and the more usual forms of generalized obesity so that the characteristic example is rare.

An insufficiency of the posterior lobe of the hypophysis is too often thought to be the etiological factor in the production of obesity. Cushing[21] experimentally produced increased fat deposits in animals by removing the posterior lobe, explaining the results on a disturbance of carbohydrate metabolism. Other investigators have attributed such obesity to lesions of the nervous system in the region of the hypophysis. In the present state of our knowledge, with the presence of a normal sella turcica and with the absence of nervous symptoms produced by involvement of the infundibular region, the pituitary origin of obesity can be only a hypothesis.

That the existence of an obesity of pituitary origin is far from an established fact emphasizes the uncertainty of action of pituitary extract in the treatment of fat children. There is considerable variation of opinion regarding the treatment of pituitary obesity. Some years ago Cushing[21] stated that laboratory animals usually lose weight when given protracted treatment with posterior lobe extract. Englebach[20] broadened that statement to include all human beings suffering from obesity thought to be due to pituitary dysfunction and advised the intramuscular administration in all such cases of pituitrin, the posterior lobe hormone, together with the pituitary sex hormone of the anterior lobe. Oral administration of desiccated pituitary substance was advised in conjunction with the preparations given intramuscularly and those cases which had an additional thyroid involvement were given desiccated thyroid. Carlson,[22] however, emphasized the uselessness of oral administration of all glandular products available at the present time, with the exception of desiccated thyroid.

Englebach firmly believed that endogenous obesity does not react to diet, exercise, or hydrotherapy and thought that in at least the earlier cases of short duration, decided effect upon the excess weight is accomplished by replacement therapy without the addition of diet or other weight-reducing procedures. However, it is well to emphasize that his prescribed treatment nearly always consisted of a low caloric diet, exercise and the restriction of fluids in addition to replacement therapy.

This plan was followed in treating obese children in the out-patient department of the Children's Hospital for a period of approximately two years. Surgical pituitrin was given intramuscularly twice weekly in amounts necessary to produce the so-called intestinal reaction, causing abdominal cramps and colic followed within half an hour by defecation. Antuitrin and thyroid were given when indicated. In addition these fat children were placed on a diet of approximately 850 calories, made up of protein, 60 grams, carbohydrates, 110 grams, and

fat, 19 grams, and adequate vitamins and minerals. The majority of the fat children thus treated lost weight and for the most part the results were satisfactory. A similar satisfactory result was obtained in an occasional child who was treated with only diet and exercise. This, together with the failure to lose weight of some obese children who received replacement therapy regularly over long periods, but who on subsequent observation in the hospital or convalescent home were proved to be eating far more food than allowed on the prescribed diet, made us skeptical of the actual benefits derived from the use of the endocrine products. The use of pituitrin was discontinued, and for the past two years all cases of obesity have been treated with the same 850 calorie diet and supervised exercise in a reducing class sponsored by the department of physiotherapy. Desiccated thyroid has been given to the occasional child who, after reaching a level, could apparently lose no more on the diet and exercise regime alone. Our results appear to be just as satisfactory as in those cases given endocrine preparations.

The frequency with which diabetes is preceded by obesity suggests that the pancreas may have something to do with the storage of fat. In the past few years the use of insulin in undernourished individuals has been advocated as a weight-gaining measure. However, the excellent results reported are probably due to the hypoglycemic effect of the insulin and the subsequent hunger and increased appetite rather than to any direct effect on fat metabolism.

The rôle of the remaining glands of internal secretion is still more doubtful. Thus one is forced to agree with Wilder[12] that "when all is said on the score of the endocrine glands, it leaves one with the impression that their rôle in the production of obesity has been astonishingly overestimated."

Recently evidence has been accumulating suggesting that the nervous system plays a more important rôle in fat regulation than the endocrine glands. Such affections of the brain as tumors, epidemic encephalitis, hydrocephalus, and chronic meningitis sometimes are accompanied by a sudden increase in body weight. These patients have the usual symptoms of the brain lesion which usually occurs in the floor of the third ventricle or in the infundibular region where there are visceral nuclei regulating the metabolism of fats, carbohydrates and water. In hydrocephalus obesity probably only occurs in those instances in which there is a dilatation of the third ventricle resulting from a closure of the aqueduct of Sylvius, connecting the third and fourth ventricles, the communication between the lateral and third ventricles remaining open.

Leschke[23] recently reported a series of 149 autopsies on cases of adiposogenital dystrophy. He reported only twenty-one in which the

pituitary body alone seemed to be involved. In the remaining 128 cases there was definite pathologic evidence of injury to the neighborhood structures in the diencephalon with no apparent change in the pituitary body. Philip Smith[24] has demonstrated in animals that removal of the hypophysis without injury of the surrounding brain tissue will not cause obesity. His experiments further demonstrated that when the diencephalon definitely is injured, obesity usually results regardless of whether or not the hypophysis is damaged.

Many observers have noted the occurrence of obesity after typhoid fever and other infectious diseases. The abrupt development of obesity after an acute infection involving the central nervous system points to the possibility of inflammatory changes in the region of the pituitary body and the visceral nuclei. Raab[25] reported an example of obesity following post-vaccinal encephalitis. Adiposity often follows lethargic encephalitis while the pathology of this disease involves chiefly the mesencephalon and diencephalon, the hypophysis rarely being affected. Moncrieff[26] has recently reported two cases of marked obesity occurring after the acute stage of chorea. Coburn[27] mentioned obesity following chorea in seven of his carefully studied 3,000 rheumatic patients and states that "this striking development of adiposity is perhaps an objective indication of cerebral changes, possibly in the region of the hypophysis."

Such symptoms as polydipsia and polyuria, unusual lethargy or disturbance of heat regulation frequently are associated with obesity following injuries or pathologic changes in the diencephalon. Wilder[12] was of the opinion that "the theory of abnormal central irritability is more probable than any of the explanations of obesity based on postulations of endocrine disturbance or abnormal economy of energy."

TREATMENT

The prevention of obesity would be given more attention if people realized how much easier it is to avoid gaining an excess of weight than it is to reduce the weight once it has been put on. The modern mother in her anxiety to see her child grow and develop normally often is responsible for his gradual acquisition of a large appetite. She instinctively feeds her child all she possibly can. Such an attitude may result in the child's acquiring a permanent habit of eating more than his body requires. Eating is one of the favorite indoor sports of America. It is encouraged by the art of cooking which has as its sole object the endeavor to get us to eat more than we should. Previous to the present economic collapse, overeating had become a habit with millions of adults as well as children, yet most of us escaped adiposity.

Should obesity in children be ignored? Is the reduction in weight of the obese child worth all this effort? We are not certain whether

all the degenerative changes that accompany adiposity in the adult occur in childhood. But we do know that obese children are poorer surgical risks, that they are more prone to develop pneumonia and pulmonary complications, and that diabetes is a potentiality to be considered. Faulty posture, usually a lumbar lordosis, and various orthopedic abnormalities of the feet are aggravated or initiated by obesity. Fat children are the victims of continuous teasing, which in some is apt to initiate a feeling of inferiority resulting in serious behavior problems. The esthetic value of a slim body, of prime importance to the young co-ed, is not the least consequential of all the reasons for maintaining normal weight in a child.

The diet is the all-important factor in the treatment of obesity in children. It should be sufficiently low in calories to insure a negative energy balance. Enough protein should be prescribed to assure a nitrogen balance, to protect the body proteins, and to allow for normal growth and development. The diet should include an ample supply of the vitamins as well as mineral salts, especially calcium and iron. Foods which allay hunger and give the greatest satisfaction are most desirable. Meat, for instance, sticks to the ribs the longest of the protein foods, according to McLester.[28] He further points out that hard-boiled eggs have a higher satiety value than soft-boiled eggs and potatoes are preferable to bread for the same reason.

Various types of diets have been suggested, but in the final analysis, providing sufficient protein is consumed to assure a nitrogen balance, it matters little just how the diet is made up, the principle of all obesity diets being a reduction of the total caloric intake to such a level that the fat stored in the body will be called upon to make up the daily energy requirements. The cooperation of the patient and both parents is most essential in seeing that the obese child adheres to the dietary regime.

Veeder[29] maintained that the rapid growth which takes place at the pre-adolescent and early adolescent period tends automatically to correct the obesity, if the child's dietary can be controlled. He favored maintenance of the obese child's weight permitting the patient to grow into it, so to speak, rather than attempting a marked reduction of the weight.

One should explain to the parents beforehand that the sudden losses or gains usually are due to changes in the water content of the body, not change in the amount of fatty tissue. The loss of several pounds during a strenuous afternoon of play on a hot summer day is usually regained within a day or two through increased water intake. The studies of Friese and Jahr[30] have proved conclusively that fat children show no greater tendency to retain water than do normal children and that the restriction of the fluid intake is of no importance in the treatment of obesity.

As an adjuvant of dietotherapy, exercise undoubtedly is of great importance. Calesthenics, walking, tennis, roller skating, swimming, or any form of muscular activity available to the child should be encouraged. The cooperation of our physiotherapy department in maintaining the reducing class has been very helpful. The obese child characteristically is lazy and it is sometimes doubtful whether he is carrying out his prescribed exercises at home; in the reducing class he is put through his paces on at least two days a week. But one should remember that muscular exercise increases appetite and the benefits of increased caloric expenditure resulting from the exercise may be cancelled by an increased caloric intake not called for on the deitary plan.

Massage seems as useless in treating the fat child as it is in the adult, although it perhaps increases the sense of well-being. Barker[4] remarked that "massage does nothing toward the removal of fat in the patient, though it may do so for the masseur."

The medicinal treatment of obesity seems of little importance even though the use of various endocrine preparations has been all too common. Every obese child can be made to lose weight on diet and exercise alone, provided there is the proper cooperation between the child, his parents and the doctor. Occasionally, the addition of desiccated thyroid by mouth is advantageous as an adjunct to diet and exercise in the child who, on the usual regime, has established a level and is unable to further reduce his weight without the catabolic effect of the thyroid. This is a drug to be respected, however, and should not be used indiscriminately in every case of obesity. When thyroid products are prescribed, the patient must be observed frequently for symptoms of thyroid intoxication.

While others have reported the successful use of hypophyseal preparations in the treatment of dystrophia adiposogenitalis and other forms of obesity in children, their results would appear more convincing if the endocrine replacement therapy were the sole method of approach. However, increased muscular activity and a lowered caloric intake are the all-important factors in any successful treatment of obesity, regardless of its etiology. If the overweight child can be reduced to his normal on diet and exercise alone, with perhaps occasionally the use of small doses of thyroid extract by mouth, it would seem unwise to resort to the fear, discomfort, pain and expense of injecting pituitary or other glandular preparations.

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NONSPECIFIC INFECTIOUS GRANULOMA AND CARCINOID OF THE APPENDIX

Report of a Case

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NONSPECIFIC infectious granuloma of the appendix is very infrequent in adults and extremely rare in children. In a fairly careful review of the literature only fourteen cases were found in which a granuloma involved the appendix. A summary of these cases is shown in Table I.

Table I

AUTHOR	AGE	SEX	TREATMENT	RESULT
Regling,[1] 1902	59 yr.	M	Tumor, appendix, portion of ileum and cecum removed.	Death
Gangitano,[2] 1909	32 yr.	F	Tumor and appendix removed.	Recovery
Goto,[3] 1912	52 yr.	M	Tumor and appendix removed.	Recovery
	59 yr.	M	Tumor and appendix removed.	Recovery
Läwen,[4] 1914	51 yr.	F	Tumor, appendix, portion of ileum and cecum removed. Lateral anastomosis of ileum to transverse colon.	Recovery
Tietze,[5] 1917	25 yr.	M	Drained.	Recovery
Körte,[6] 1921	33 yr.	Unstated	Tumor, appendix, portion of ileum and cecum removed.	Recovery
	38 yr.	Unstated	Appendix removed. Tumor not removed.	Recovery
	50 yr.	Unstated	Tumor, portion of ileum and cecum removed. Lateral anastomosis of ileum to cecum. Appendix not isolated.	Recovery
Gunn and Howard,[7] 1931	41 yr.	M	Tumor and appendix removed.	Recovery
Eggers,[8] 1933	64 yr.	M	Ileocolostomy. Tumor not removed. X-ray therapy.	Recovery
Gowen and Van Alstyne,[9] 1933	22 yr.	M	Tumor and appendix removed.	Recovery
Janssen,[10] 1933	21 yr.	F	Appendix removed. Tumor not removed.	Recovery
Morris,[11] 1933	23 yr.	M	Tumor and appendix removed. Colocolostomy about the obstruction of transverse colon.	Recovery

In this group of fourteen cases there was no record found of any in the age of childhood the youngest patient being a woman, twenty-one years old—the case reported by Janssen.[10]

Carcinoid tumors in children, on the other hand, are well known, but no record could be found of a carcinoid of the appendix associated with

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a granuloma. The following case is of interest because the granuloma and carcinoid tumors were found in the appendix of a girl, aged eleven years:

H. M., a girl aged eleven years, was admitted to the Children's Memorial Hospital, Dec. 7, 1932, complaining of pain in the abdomen, vomiting, and fever. The pain associated with vomiting began nine days before admission and, at the onset, was generalized throughout the abdomen. The temperature before admission was as high as 101.2° F. The patient was given milk of magnesia on the first day of her illness, and her bowels moved once after this. Four days after the onset her condition improved so that she attended school for one-half day, but shortly after the abdominal pain gradually became more severe and settled in the right part of her abdomen.

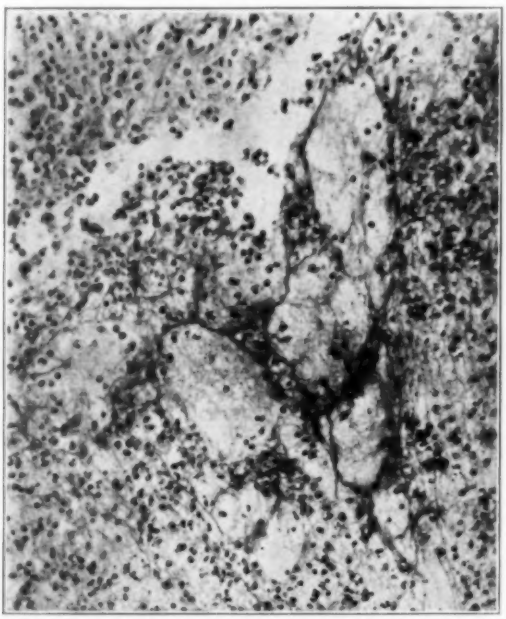

Fig. 1.—Granuloma in the omentum showing necrosis and granulation tissue; ×200.

Her previous history was relatively unimportant.

Physical examination was negative except for the abdominal findings. There was tenderness over McBurney's point and just above it. The right lower abdominal wall was rigid. No mass was felt on rectal examination. Blood examination revealed 18,800 leucocytes, with 88 per cent polymorphonuclear forms. The urine examination showed nothing abnormal, and no gonococci were found in the vaginal smears. The temperature was 101.9° F., pulse 100, and respiration 24.

A diagnosis of acute appendicitis was made, and four hours after admission the patient was operated upon under nitrous oxide anesthesia. On opening the abdomen through a McBurney's incision a large, firm, nodular mass 10 cm. in diameter was

encountered, which surrounded the distal and middle portions of the appendix. This mass was attached to the anterior and lateral abdominal walls and to the omentum. The proximal portion of the appendix, which was not involved in this mass, was ligated at the base and amputated. The stump was cauterized but not invaginated because of technical difficulties. The mass was freed with some difficulty, and some capillary hemorrhage, which was controlled by warm packs, ensued. A definite small amount of pus was encountered during the operation. Two cigarette drainage tubes were inserted down to the region from which the mass was removed, and the incision closed. The dressings were changed once during the night following the operation because of hemorrhage. The day following the operation the patient developed marked abdominal pain, distention, and rigidity, a temperature of 106°, and died with signs of acute peritonitis.

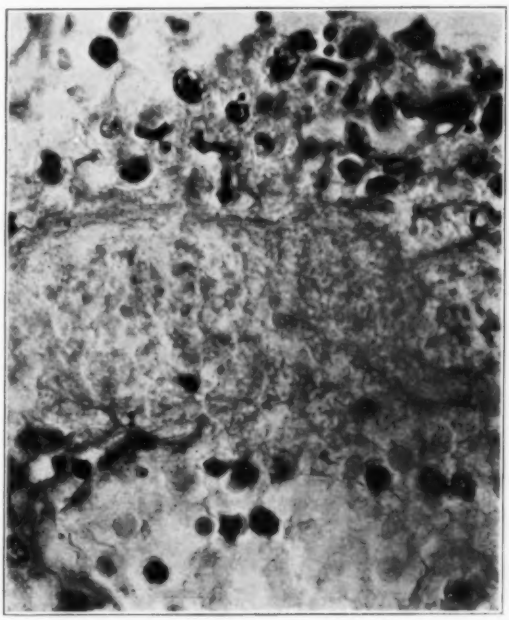

Fig. 2.—Granuloma showing necrosis of omentum with leukocytes and fibroblasts; ×1000.

A necropsy (limited to the trunk) revealed a bilateral terminal hypostatic bronchopneumonia, acute generalized fibrinopurulent peritonitis *(Streptococcus viridans)*, and a small granuloma in the omentum at the site of operation. The granulomatous tissue measured 2 cm. × 2 cm. and was apparently a portion of the mass, which was overlooked at the time of operation.

The mass removed at operation measured 10 cm. × 5.5 cm. × 3 cm. About one-half of its surface consisted of a sharply defined, reddish brown portion, the central part of which was friable and easily torn. The rest of the surface was made up of light brown to yellow nodules of omentum, in the crevices of which were injected blood vessels. On the broad, flat surface made by sectioning longitudinally, three-fourths of the specimen was light gray to brown and streaked with yellow nodules. The

appendix, which was retained within the middle and anterior portion of the mass of tissue, measured 10 mm. in diameter. The entire central portion of this appendix was light brown to yellow, its periphery pearly gray. In the middle of the wall of the appendix, there was a discrete, gray nodule measuring 2 mm. in diameter. This was all encased in a reddish brown, soft, edematous mass of tissue which was evidently friable granulation tissue and omentum.

Microscopic examination of the tissue showed the mucosa of the appendix was everywhere intact. In the submucosa were isolated neutrophilic polymorphonuclear leucocytes and active hyperplasia of the germinating follicles of the lymphoid stroma.

The tunica muscularis and serosa, however, were markedly distended with serum and a huge infiltration of polymorphonuclear leucocytes in various stages of de-

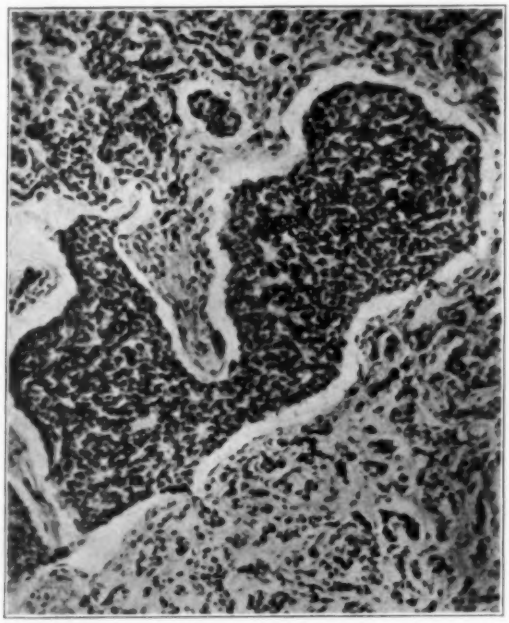

Fig. 3.—Carcinoid cells in strands and clumps growing in the appendix; ×200.

generation. In places, clumps of these leucocytes were present as in suppuration. The fatty areolar tissue of the omentum was intimately fused around the entire appendix and so diffusely infiltrated with this inflammatory exudate that it was difficult to decide as to which portion was appendix or omentum (Figs. 1 and 2). Isolated foreign body giant-cells were present in the serosa and in the omentum.

In the peripheral portions of the submucosa of the appendix, there were clumps and strands of cells with large, oval to round nuclei (Figs. 3 and 4). The nuclear chromatin was present as coarse granules distributed throughout the nucleus but possibly more abundant near the periphery. No definite mitotic figures were present. The nuclei were about two times the size of those of the lymphoid tissue of the submucosa. Where these large nuclei occurred in single strands which ramified through the submucosa, they were enmeshed in a fibroblastic reticulum.

COMMENT

It seems unnecessary to discuss the different features of nonspecific granuloma in detail, because they have been enumerated admirably by Andrews,[12] Birt and Fischer,[13] Braun,[14] Coffen,[15] Eisenberg,[16] Füth,[17] Gordon,[18] Goto,[3] Graser,[19] Jaffe,[20] Koch,[21] Körte,[6] Lejars,[22] Mock,[23] Monsarrat,[24] Morian,[25] Moynihan,[26] Prima,[27] Tietze,[5] Wilensky and Moschowitz,[28] and others. A few additional comments are sufficient.

As far back as 1898, Gassenbaur reported a case of an inflammatory tumor of a diverticulum which he at first thought was a carcinoma, but

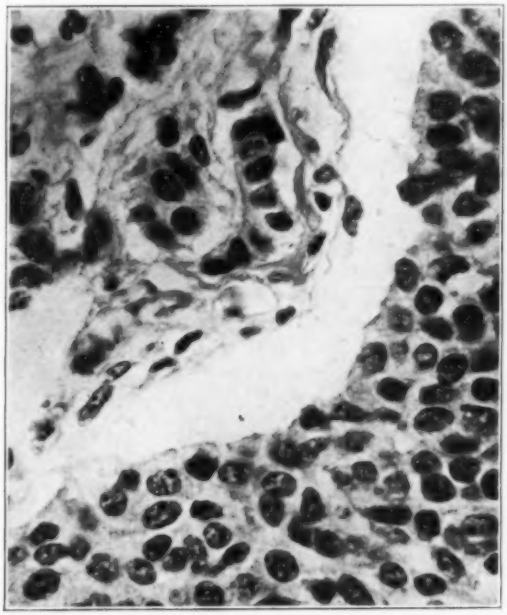

Fig. 4.—Carcinoid showing nuclei and cytoplasm with fibroblastic reticulum; ×1000.

which later proved to be a nonspecific infectious granuloma. In 1908, Heinrich Braun[14] reported his classic collection of inflammatory tumors of the bowel, which are now designated as nonspecific infectious granuloma. There were, however, a number of cases reported before Braun's contribution.

Nonspecific infectious granuloma occurs in children in regions other than the appendix. Körte[6] reported a case of granuloma of the ileum in a child aged eight years and Prima[27] reported a case with a granuloma of the back in a child aged three months, occurring probably as a result of a puncture of the amnion. Granulomata occur in other regions than the gastrointestinal tract as shown by Prima's[27] case involving the back,

numerous cases that have been reported involving the female genital organs, and the case reported by Hufnagl[29] involving the abdominal muscles and bladder. Körte[6] stated that the majority of these lesions are in the colon. Some of the granulomata follow appendectomy, the subsequent involvement often being in the cecum or ileum, or both. In 107 cases of granulomata of the abdominal organs, there were eight that were definitely stated to have followed appendectomy.

The granulomatous tumor consists of a hyperplastic mass, often occurring at the site of some preceding lesion, as a gastric ulcer, appendicitis, bowel ulcer, or of a foreign body. It represents a destructive combined with a reparative process. Necrosis occurs accompanied by a productive proliferation composed of round cell infiltration, leucocytes, fibroblasts, connective tissue stroma, new blood vessels, giant-cells, and often mast-cells. Finally a definite, tumorlike mass, a granuloma, forms which may become the size of a grapefruit.

The symptoms are those of local infection, bowel obstruction, and constitutional reactions. Pain, tenderness, rigidity, and a mass are often present locally. Intestinal obstruction occurs if the tumor encroaches on the bowel lumen. The constitutional reactions include fever, leucocytosis, and loss of weight.

The diagnosis is rarely made except at operation or necropsy. These cases have often been diagnosed as carcinoma, syphilis, or hyperplastic tuberculosis of the bowel. More rarely they have been confused with amebic disease, actinomycosis, and bilharziasis (Tietze[5]).

A diagnosis of carcinoma has frequently been made and a fatal prognosis given, and yet the process has terminated in a complete recovery. In a number of cases reported, the granulomata disappeared spontaneously. Recurrences after apparently complete removal have been noted in many patients.

The treatment of these cases is essentially surgical. Often simple exposure of the mass, drainage, or a sidetracking operation of the intestine results in a disappearance of the tumor. Local removal, if possible, is advisable except when pus is present, in which case drainage is advisable. If bowel obstruction is present enterostomy or entero-enterostomy is recommended.

Carcinoid tumors were first separated from carcinomas by Lubarsch in 1888. Oberndorfer[30] proposed the name "carcinoid" in 1907. They have been ably described by a number of authors.[30, 31, 32, 33, 34, 35] These tumors have been referred to as "chromaffin" because they stain well with chrome salts. They have also been known as "argentaffin" tumors since Gosset and Masson[31] found that the granules of their cells reduce ammoniacal solutions of silver.

The tumors according to McGlannan and McCleary[35] and several other observers originate from certain chromaffin cells found at the base of

Lieberkühn's crypts. It has been thought that they arise from sympathetic nerve tissue but Masson[31] opposed this view. He believed they resulted from proliferation of intranervous argentaffin cells of the neurocrine type. They were at one time thought to be pancreatic rests (Saltykow[36]). Also, they have been considered as malformations. Bunting's[37] view was that they were analogous to Krompecher's basal cell carcinomas of the skin. According to Forbus[32] they occur in 0.4 per cent of appendices removed at operation. Masson[31] found fifty carcinoid tumors in 1,200 appendices which he examined.

Carcinoids in general are comparatively small tumors. They are rarely more than a centimeter in diameter (Raiford[34]) and may be so small as to be invisible to the naked eye. In regard to malignancy, it seems that they are comparatively benign as Stewart and Taylor[38] in 1926, in an extensive review of the literature, found only eighteen cases of carcinoid tumors with metastases. In those cases, metastases were found in the regional lymph nodes, mesentery, liver, peritoneum and pleura.

Because of their small size, it is doubtful whether these tumors could cause symptoms referable to the appendix unless they should obstruct the lumen with a resulting inflammatory reaction. It might be suggested that carcinoid tumors may be more commonly the primary factor in appendicitis than is generally supposed. If complete sections were made of all appendices removed more carcinoids would probably be found because many are microscopic in size.

Their treatment, of course, is the usual appendectomy.

The patient reported here died from a generalized peritonitis, probably as a result of overlooking a small portion of the infected granuloma attached to the omentum. However, another possibility is that the fatal peritonitis resulted from the free pus encountered at the time of operation. Still another possibility is that the peritonitis had already begun before the time of operation. This last supposititon is supported by the fact that there was evidence of a severe infection during the nine days preceding the operation. Mock[23] stated that as a rule a granuloma soon becomes and remains sterile.

The probable sequence of events in this patient is as follows: the carcinoid growing in the wall of the appendix finally produced an obstruction of the lumen with resulting inflammation distal to that point; a rupture occurred soon after with localization of the infection; and ultimately a granuloma developed and grew into the omentum.

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INSULIN IN UNDERNOURISHED NONDIABETIC CHILDREN

An Attempt to Induce Gain in Weight

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RECENT literature on the uses of insulin is conspicuous for the numerous references to it as an appetizer and tonic. Many of the reports make conclusive statements as to its efficacy in this direction. These reports are principally confined to the use of insulin in adults, where appreciable gains in weight, ranging as high as four to twenty-two pounds have been made in from one to four weeks.[1, 2, 3] At the same time tremendous improvement in appetite, morale, and well-being have been effected. The efficacy of insulin has been particularly noted in the anorexia that accompanies chronic wasting diseases as tuberculosis, etc.,[2, 4] but it has also been reported as successful in overcoming the anorexia and subsequent malnutrition resulting from other conditions. The range of doses has been quite extreme, varying from five units even to forty units, two or three times a day. On the other hand, smaller doses, given at more frequent intervals, have been preferred by other investigators.

These results have been explained on the effect of insulin on gastric motility and on gastric, biliary and pancreatic secretions. Bulatao and Carlson[5] have shown an increase in gastric tonus and in frequency and height of gastric contractions in dogs, coming on after an hour of gastric quiescence. They explain this initial inactivity as due to inhibition by insulin, the tetany being due to the subsequent hypoglycemia. Quigley, Johnson and Solomon[6] found an increase in gastric motility in humans after insulin, accompanied by an increase in gastric tonus, prolonged hunger period, and hunger sensations. These effects were offset by the administration of dextrose or the injection of adrenalin. They were not inhibited, however, by unpleasant sensations, nausea, etc. Regan,[7] using dogs, corroborated the present conception of an inhibition of gastric motility by insulin for a period varying from fifteen to sixty minutes, followed by gastric hypermotility coincident with a demonstrated hypoglycemia. Moreover, Okada et al.[8] point out an increase in gastric, biliary and pancreatic secretions as a result of what they call the "humoro neural" effect of insulin, in contradistinction to the "humoral" effect of food. This effect they likewise ascribe to hypoglycemia. The work of Macleod, Magee and Middleton[9] indicates that the results may be due to an in-

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creased food consumption. Working with pigs they found that "runts" made better gains with insulin than without, but healthy animals gained equally well in the long run with or without insulin. The food consumption was carefully measured, showing an increased intake with insulin.

Insulin, as an appetizer, has not been used much in children. Pitfield,[10] who was the first to employ it in infants, gave it to two babies four and five months of age respectively, who were suffering from malnutrition, with encouraging results. Subsequently Marriott[11] used it with good effect, together with glucose parenterally, in athreptic infants. He employed it only in extreme cases. Fischer and Rogatz[12] used insulin in twenty-seven infants ranging from three weeks to thirteen months of age, and suffering from various degrees of malnutrition. They considered its use beneficial and even life-saving in some cases. Tisdall et al.[13] also gave insulin to infants under one year, most of whom were suffering from malnutrition. They cast a discordant note into the tune of insulin efficacy in malnutrition by reminding that since marasmic infants have a lower blood sugar than normal infants, insulin may be dangerous at times. Moreover, since they metabolize glucose at a faster rate than normal infants, the administration of insulin is unnecessary. Their contention has subsequently been given support by the work of Wilson, Levine and Gottschall,[14] who showed that there was no fundamental difference in carbohydrate metabolism between normal and marasmic infants; that marasmic infants suffered no demonstrable defect of carbohydrate metabolism. They found that the amount of carbohydrate burned by either normal or marasmic infants was essentially the same whether insulin was or was not administered. The work of Barbour[15] is one of the few instances of the administration of insulin in older children to increase their weight. He used three units three times a day before meals in children under two years, and five units three times a day in older children. He found consistent improvement in weight and well-being, with best results in those cases suffering from the greatest degree of malnutrition. He could discern no untoward results.

In an attempt to evaluate the efficacy of insulin in older children and to determine the optimum dosage, the following studies were undertaken. One group of five boys and another of six boys, ranging from eleven to fourteen years of age, were observed. They were all underweight from 4 to 20 per cent below the accepted standards for their height and age.

FIRST SERIES

Five boys, wards of the Brooklyn Hebrew Orphan Asylum, were chosen as subjects. The advantages of using institutional subjects are

obvious with respect to cooperation from the authorities in charge and from the children themselves. Diets are more easily and more accurately controlled. The growth curves of the children for previous years are available. Moreover, the children can be compared with the hundreds of other children not being studied, who act as controls. No physical abnormalities could be detected in the subjects after careful medical examination. They were active and cheerful. In short, they typified the youngster whom anxious mothers usually bring to the physician with the complaint of underweight and poor appetite.

Insulin injections were given twice daily, fifteen to thirty minutes before meals. In the morning they were given by the nurse in charge, in the afternoon by either one of us. The initial dose was three units twice a day, and was increased in two days to five units twice daily. This dose of five units twice a day was then given for two weeks. At the end of two weeks the dose was slowly increased to eight units twice a day, taking one week to accomplish this. For the fourth week the dose was increased in a similar way to thirteen units twice a day. During the fifth week the dose was fifteen units twice a day. The latter dose was also given during the sixth and seventh weeks of insulin administration, but here the injections were given one hour before meals in order to produce a maximum degree of hypoglycemia by the time food was taken. At this time the gastric hypermotility due to hypoglycemia should be manifested.

The diets which the subjects received were carefully supervised with respect to quantity, so that as much food was served as an augmented appetite might require. The fare was of the usual type, the only deviation from routine being the candy given in the event of hypoglycemia. Care was taken that the candy should not be eaten until after mealtimes, unless symptoms supervened.

Several menus served the children at the institution where this work was carried out are here set down. They have been picked at random:

Breakfast	Oatmeal, bread, butter, cocoa, sugar.
Lunch	Hamburger loaf, mashed potatoes, peas, carrots, apples, bread.
Dinner	Baked beans, bread, butter, chocolate pudding, milk.
Breakfast	Wheatena, bread, butter, cocoa, sugar.
Lunch	Spaghetti, tomato sauce, bread, jam, milk, cookies.
Dinner	Salmon salad, mashed potatoes, rolls, butter, milk, fresh fruit, cake, bread.
Breakfast	Two boiled eggs, bread, butter, cocoa, sugar.
Lunch	Pot cheese, sour cream, bread, jam, milk, fruit, jello.
Dinner	Boiled beef, parsley potatoes, string beans, bananas, bread.

Staples, such as bread, butter, milk, fruit, etc., were supplied in abundance. This was repeatedly observed by the writers. Tomato juice was served every day, as well as vitamin D in some form.

Such a diet, plain but plentiful, can be seen to be adequate in vitamin and mineral content. It provides a minimum of from 2,400 to 2,800 calories. When calculated in terms of the individual foods, it is found that approximately 50 per cent of the total calories is supplied by carbohydrate, and 15 to 20 per cent by protein. The diet also provides between three to four grams of protein per kilogram of body weight. Such a diet is more than sufficient to induce normal growth and gain in weight.

The boys were carefully weighed at least once a week by each of us as a check, and their heights taken. Note was made of any subjective or objective symptoms, and of any changes in well-being, appetite, etc. After cessation of insulin administration, the weighings were still continued weekly.

SECOND SERIES

Profiting by some of our observations in the preceding series, a second series of injections was undertaken in a new group of six boys. These were similar in type to the boys in the other group. One of the boys was withdrawn after one week of insulin because his mother, a nurse, objected to the injections. The other five boys were given five units of insulin twice a day, one hour before meals. Within one week the dose was rapidly increased to fifteen units twice a day. This dose, given one hour before meals, was continued until the end of the experiment, which lasted one month. As in the preceding experiment, the subjects were weighed naked once a week and always at the same time of day. Their heights were also recorded; here also all symptoms were carefully watched for.

At this time, eight other boys were chosen as controls. Their weights had been found to fall just within the accepted normals for age and height. On the strength of their previous records, it was reasonable to expect that they would not make unusual gains. They were subjected to the same routine as the other boys, but were given no insulin and no candy. Their diet coincided with that given the insulin subjects. They were also weighed at intervals, the last weighing being made about two months after the first.

RESULTS

The boys in the first group made no significant gain on doses under ten units twice a day. At that dose, one lad gained one and one-half pounds in a week. He had complained, more than the others, of dizziness after the injections. On fifteen units twice a day the greatest gain occurred, the maximum being one and one-fourth to one and one-half pounds during any week. Yet, while receiving this dose, two of the subjects in the first series lost one-fourth and one-half

pound respectively. The average gain per boy in this series for the entire seven weeks of insulin administration was two pounds. This figure indicates a somewhat higher gain than that which actually occurred, because one boy who was underweight for his height only because he was growing rapidly, gained four pounds, thus raising the average gain from one and one-half to two pounds. Every boy weighed more at the end of the period of observation than at its beginning. The smallest gain was one pound.

Although the boys in the second group had received larger doses of insulin, the average gain during the month of observation was one-fourth pound. This figure is a bit low because two of the subjects had failed to gain. In fact, they had actually lost one-half and one pound respectively by the end of the experiment. The greatest gain made in this series was only one and one-fourth pounds after four weeks of insulin, and this in only one boy.

As has already been intimated, the gains were not progressive. Sometimes they followed a previous loss in weight, or the entire gain might be wiped out by an equal or even greater loss the following week. Some subjects lost weight at times even on the larger doses of fifteen units twice a day. It should be said, however, that the losses were never consecutive, but were usually made up for by an equal gain. The rate of gain did not differ whether the injections were given one-fourth hour or one hour before meals. The largest gain per week in either series was one and one-half pounds, but it is obvious that such a gain was never repeated. There was an absence in our subjects of any noticeable changes in appetite, well-being, or mental attitude. Increased consumption of food was not apparent. It is interesting to note that hypoglycemic reactions often caused enough dizziness to produce actual anorexia. These reactions took the form of dizziness, pallor, perspiration, faintness, hunger, and anorexia in that order of frequency of occurrence. However, these symptoms were not severe, and did not interfere very much with the boys' normal activities.

The gains made, meager as they were, began to disappear almost as soon as the injections were stopped. Within one month after cessation of insulin all the boys but one were back to their previous weights. The latter lost one and one-fourth pounds after insulin was stopped, and then began to gain spontaneously. Many of the weights even went below their starting levels. Changes in height were not apparent, except in the one boy of the first series who had gained four pounds in weight. The latter grew one inch in seven weeks.

The eight control subjects made an average gain of one and one-eighth pounds during the time this experiment was being conducted. Three of the boys lost from one-fourth to one-half pound during this

time, while the other five gained from one-half to three and three-fourth pounds. This result, without insulin, coincides fairly well with the results in the insulin-treated group.

These findings have been summarized in Table I.

TABLE I

WEEKLY CHANGES IN WEIGHT

FIRST SERIES

		INSULIN								AFTER INSULIN				
SUBJECT	AVER. WT.	1ST WK.	2ND WK.	3RD WK.	4TH WK.	5TH WK.	6TH WK.	7TH WK.	NET CHANGE	1ST WK.	2ND WK.	3RD WK.	4TH WK.	5TH WK.
L. B.	55¾	55¼	56	55¾	56¾	56½	58	57¾	2	56¼	56	56¼	56	55¼
I. F.	64¼	64½	64¼	64	64½	65¾	65	65	¾	64½	64½	63½	63½	63½
N. F.	65¾	66½	66	66¼	66¾	68½	68½	67½	1¾	67¾	66¾	67¼	67	67½
O. K.	67½	67½	66	67½	68½	67¾	68¼	69½	1¾	68¼	67	67½	67¼	66½
W. S.	79¾	81½	80¾	82½	83¼	84½	84¼	83¾	4	83¾	83¼	84¼	84¼	80¾

SECOND SERIES

		INSULIN					AFTER INSULIN		
SUBJECT	AVERAGE WEIGHT	1ST WEEK	2ND WEEK	3RD WEEK	4TH WEEK	NET CHANGE	1ST WEEK	2ND WEEK	3RD WEEK
S. N.	70¾	71¼	73½	72	72	1¼	72¼	71½	70¾
M. P.	71	71¾		71½	70	−1	69	71½	71
S. F.	100¾	101	101½	102	100¼	− ½	101¼	102	102
J. B.	71¼	72¼	73½	73	72¼	1	71¾	72½	72½
L. A.	69¾	69¼	68¾	70	70¼	½	68¾	68¾	69¼

CONCLUSIONS

1. Insulin given to nondiabetic children in doses under ten units twice a day causes no acceleration of the rate of gain in weight. No subjective or grossly objective effects are produced.

2. Doses of ten units twice a day have but a slight accelerating effect, and doses of fifteen units twice a day have a somewhat more marked accelerating effect upon the rate of gain in weight. The total gains are small.

3. The gains in weight which are induced by these doses disappear within one month after cessation of insulin.

4. The results do not warrant the injection of large amounts of insulin to nondiabetic children with the dangers incident to this procedure, for the purpose of inducing gain in weight.

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FATIGUE IN SCHOOL CHILDREN

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THIS study covers thirty-two school children ranging in age from seven to fifteen years who came to us with the outstanding complaint of persistent fatigue. Associated symptoms were an inability to carry on the usual school duties and a lack of interest in the customary activities in play and amusement. In each child the symptoms were sufficiently pronounced to cause anxiety and consultation with the pediatrist.

All were given a complete physical examination, which included blood chemistry and basal metabolism tests when such studies seemed indicated. The patients fall into two groups.

In Group I, twenty-two in number, there was a favorable response to adequate rest habits, the correction of small gastrointestinal disorders and other minor ailments. An important feature in a considerable number was the presence of a mental depression reflecting, perhaps, the home atmosphere, due to business troubles, which few of the heads of families have escaped during the past few years. Suggestions to the parents that business troubles be omitted in discussions before the patient and an assurance to the child that he was just as strong and well as other boys and girls aided in securing a satisfactory adjustment.

In Group II, ten in number, the story was quite different. The object of this article is to call attention to this group, emphasizing a factor in child life that would seem not fully appreciated. Among these there were seven boys and three girls. One boy was eight and one-half years old, the remaining nine ranged from twelve to fifteen years of age. An outstanding symptom was the inability to carry on the school activity. In three the changed reaction of the patient to this environment in the school and in the home were so pronounced that they represented behavior problems. Means of management that were successfully employed in Group I failed to make an impression.

Repeated basal metabolism tests demonstrated that these children in contrast to Group I were persistently minus. In all, the height-weight ratio was within the normal. In the girls, aged thirteen, fourteen, and fifteen years, menstruation had been established and was normal. In the boys there was no evidence of delayed sex characteristics. In four cases normality was established under thyroid gland administration as follows: one in two months; one in six months; one in eight months; and one in eighteen months.

In these the dysfunction was temporary. In two cases unusually rapid growth may have been a factor. Each patient was rendered able to carry on his usual activities for a given time through the use of small doses of desiccated thyroid gland. Evidently there was a temporary dysfunction or an excessive call upon the thyroid gland due to rapid growth or special effort demanded at school or in the home. In five cases we have been unable to discontinue the gland therapy; attempts have been followed by a cessation of activities, disturbed mental reactions and poor school work. In one case (Fig. 3) the desiccated thyroid has recently been discontinued. Figs. 1, 2, and 3 demonstrate the basal metabolism charts of three patients in this group.

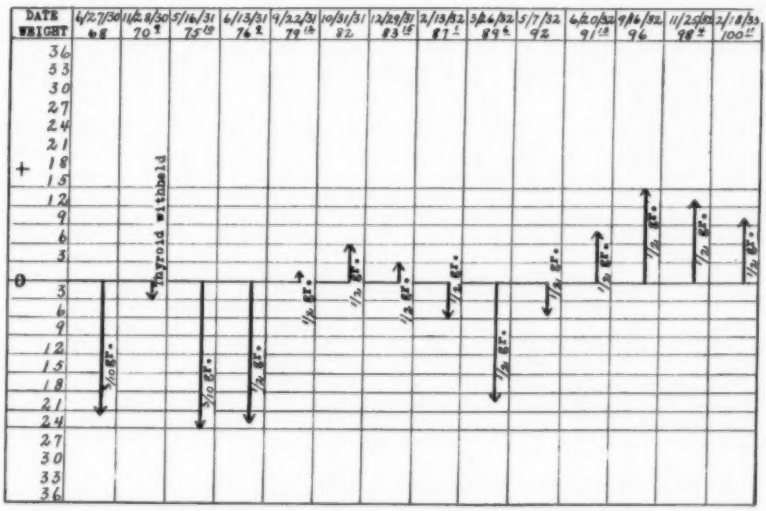

Fig. 1.—R. S., male aged twelve years and one month; the chart demonstrates basal metabolic rate and amount of desiccated thyroid administered daily.

SEX	AGE AT ONSET OF TREATMENT	GRAINS OF DESICCATED THYROID DAILY	DURATION OF TREATMENT
Male	13 yr.	1/5 to 1/2	3 yr.
Male	12 yr.	3/10 to 1/2	2 yr. 8 mo.
Male	10½ yr.	1/5 to 1/4	3 yr. 4 mo.
Male	13¼ yr.	1/2	13 mo.
Female	13 yr.	1/5 to 1/2	1 yr.
Female	13½ yr.	1/2 to 1	2 yr. 9 mo.

It will be observed in Fig. 1 that the twelve-year-old boy gained 28 pounds in weight and 8¾ inches in height during the two years and eight months he was under observation.

Fig. 2 is a chart of a girl fourteen years old, who was physically normal, but failed signally in her school work, and was quite unable

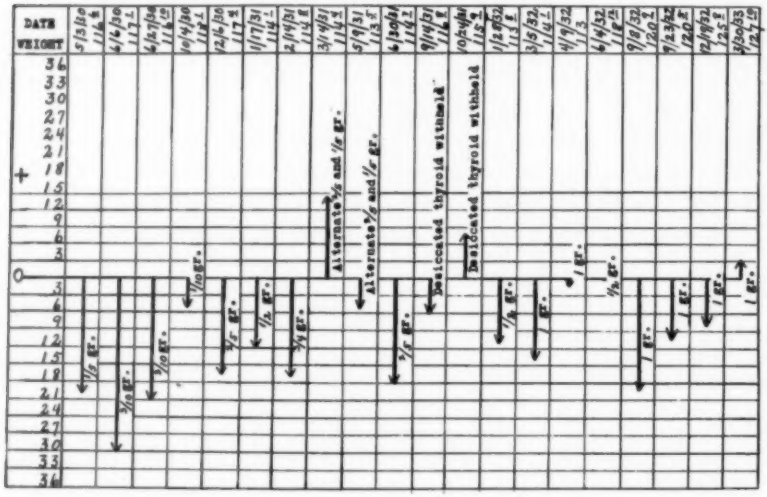

Fig. 2.—V. D., female aged thirteen years and six months; the chart demonstrates basal metabolic rate and the amount of desiccated thyroid administered daily.

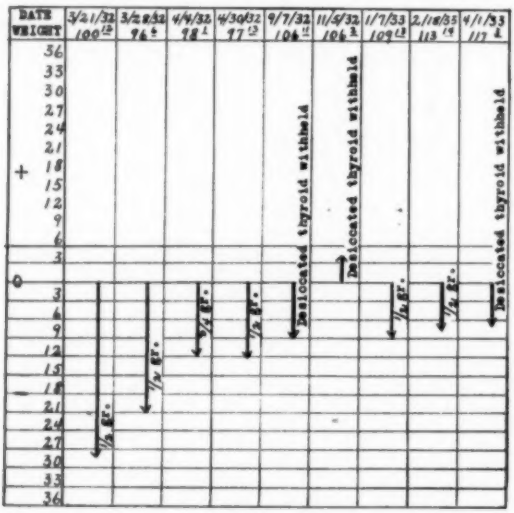

Fig. 3.—S. S., male aged thirteen years and one month; the chart demonstrates basal metabolic rate and amount of desiccated thyroid administered daily.

to carry on effort in any direction. She was a source of no little anxiety to her teachers and immediate family. As a result of desic-

cated thyroid administration, she took her place in the class and, for efficiency in her studies, won a scholarship to a private school for girls.

In Fig. 3 is shown the chart of a thirteen-year-old boy in whom we have recently discontinued the use of desiccated thyroid medication. It will be observed he has gained 18½ pounds in weight and 3⅛ inches in height in thirteen months. We feel the discontinuance of the thyroid for this boy was warranted on account of the complaint of dizziness and headaches, and an apparent return to normality in his school and family reactions. There had been a complaint of a similar nature four months prior to this when the thyroid medication was discontinued. However, the resumption of its use was required on account of a return of the mental disability.

COMMENT

Our study covers thirty-two children in whom disease of any nature was proved absent. They came to us from different sections of the country and for one reason only, that of fatigue—an absence of initiative and capacity for effort. Twenty-two were permanently relieved through an adjustment of living conditions in the home and through the correction of small physical ailments which related particularly to activities, sleep, diet, and bowel function.

Unfavorable domestic environment was of etiologic significance in a few of the children. In ten cases repeated basal metabolism observations showed an endocrine dysfunction as a causative agent.

Particularly of interest in this group was the demonstration both clinically and by repeated metabolic observation of the potency of small thyroid dosage. This observation suggests the thought that small amounts of animal thyroid might act as an excitor of a familial tendency to thyroid dysfunction to normal efficiency.

It is to be understood in these children there was no suggestion of myxedema, no obesity, and no delay in sex characteristics. We feel that the administration of the desiccated thyroid will have to be maintained until adolescence is passed and the competitive stressful school existence has been concluded. We are also confident that if these children had not had the value of thyroid gland therapy, they would not have been able to carry on their usual school activities.

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THE USE OF OXYGEN IN THE CARE OF FEEBLE PREMATURE BABIES

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AT THE suggestion of Dr. H. E. Utter, an oxygen box as described by Burgess[1] was introduced into the nursery of the Providence Lying-In Hospital. This apparatus consists, in principle, of a box open at the top. The oxygen is admitted through tubes at the sides. Being heavier than air, it increases the oxygen content in the box. One side of the box is replaced by a rubber sheet with a hole in it, the edges of which fit tightly around the baby's abdomen, leaving his hands and shoulders inside and his lower trunk and legs outside.[2] This is described and illustrated in the original article by Burgess. We found that when oxygen was run in at the rate of one liter per minute, the percentage of oxygen in the air at the bridge of the baby's nose was about 30. This percentage was determined by the Yandell Henderson Syringe method. At first we used the box for several hours at a time on sick, newborn babies. Later a very feeble premature baby did so well in the box that she was left in for nine days. Two others received this treatment for fourteen and three days, respectively, apparently with great benefit. These three cases furnish the material for this communication.

Baby D was born January 1, 1933, nine weeks before the estimated date, weighing three and one-half pounds. There were no important abnormalities of prenatal period or labor. Since her condition was poor with some cyanosis, a mixture of oxygen and carbon dioxide was given. (Chart 1.) A little breast milk was given with an evaporated milk formula for the first week, and, after that, evaporated milk, Karo and water until the baby left the hospital.

On the eighteenth day of life the baby's condition became very poor; she could not retain food; and her color was poor. At this time she was put in the oxygen box and left there for nine days, except for intervals of a few minutes. Within twenty-four hours, her appearance had become good, and in the nine days following, she gained twelve ounces. Immediately after beginning the administration of oxygen, her temperature, which had been difficult to control, kept within satisfactory limits. Her chart tells the story clearly. She left the hospital in eight weeks, weighing five pounds. The family then left town, and we have been unable to follow the case.

Baby J was born February 12, 1933, weighing three pounds and six ounces. There were no important abnormalities of the prenatal period or labor. The baby was estimated nine weeks premature. Because her condition and color were only fair, she was put in the oxygen box immediately. She was kept in for twenty-

two of her first thirty-two days and was fed entirely on evaporated milk formulas by gavage. At fifteen weeks she weighed six and one-half pounds and was in good condition. (Chart 2.)

Baby C, born March 23, 1933, weighing three pounds and fourteen ounces, was estimated to be six weeks premature. There were no important abnormalities of the

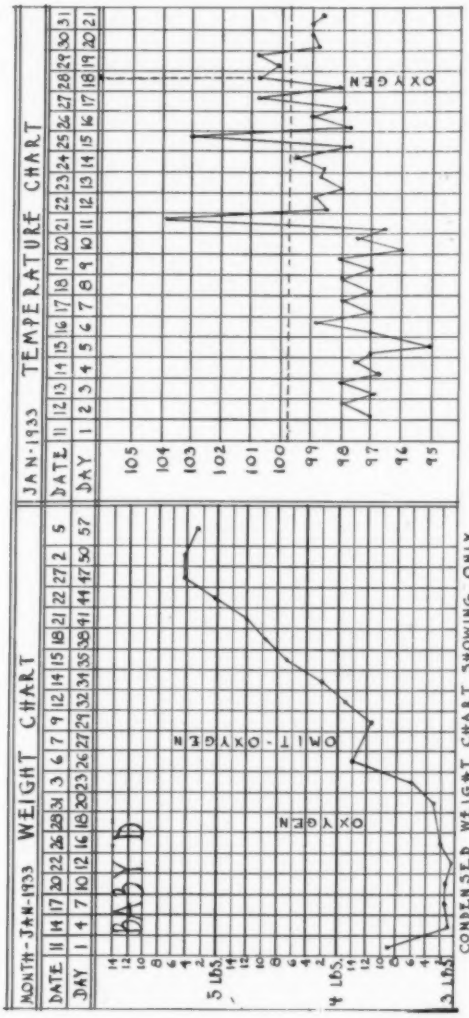

Chart 1.

prenatal period or labor. An oxygen and carbon dioxide mixture, together with artificial respiration, was necessary to start her breathing. She was sent to the premature nursery in poor condition; for the first two days, her temperature was always under 94° F. She was fed on an evaporated milk formula by gavage. From

the first day she was kept in the oxygen box. Her color was improved when the rate of oxygen flow was increased to 2½ liters per minute, or 45 per cent. Beginning on the fourth day of life, her temperature stayed almost steadily above 98° F. Oxygen was discontinued at this time because the box was needed for a sick baby.

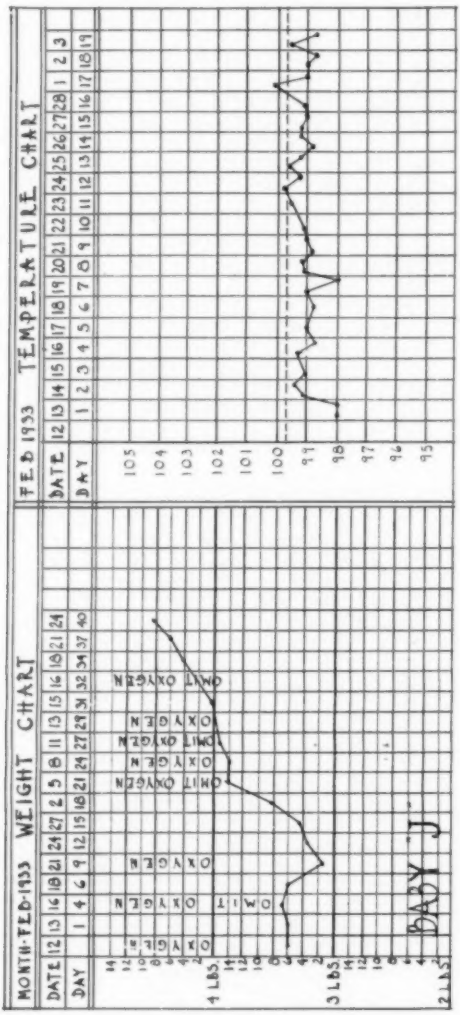

Chart 2.

Although she did not gain at first, her condition was not bad. Since then she has done well. At ten weeks she weighed five pounds ten ounces.

Charts 1, 2, and 3 show the weight and temperature charts of the three babies. The weight charts have been condensed so that they show only the days on which babies were weighed and those on which

the oxygen was given or omitted. The temperature charts show the first twenty-one days of life.

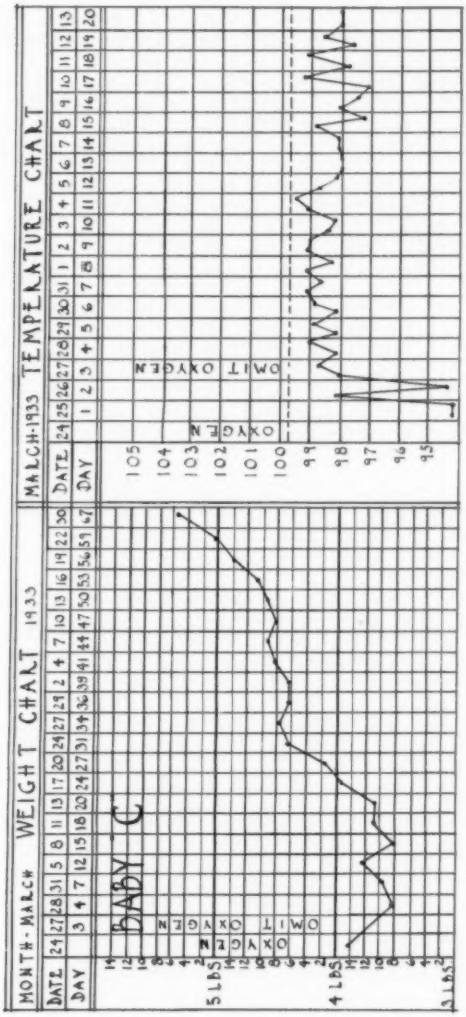

Chart 3.

SUMMARY

Three babies were kept in an oxygen box where they breathed an air with added oxygen. The improvement in their appearance and general condition was striking. They have all done well since, although before oxygen was administered, the prognosis seemed poor.

CONCLUSION

A continuous supply of oxygen seems to be of advantage in treating feeble, premature babies.

NOTE: Since the above cases have been treated, we have been using a larger box in which the entire baby can be placed.

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THE SERUM TREATMENT OF PNEUMONIA IN CHILDREN

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THIS study was carried out for two successive years up to July, 1933, in the pediatric service of Fifth Avenue Hospital. Our purpose was first to find out which types of pneumococcus are most frequently found in lobar and bronchopneumonia among children; second, to determine the mortality, length of disease, and frequency of complications among the pneumonia cases; and third, to learn whether the administration of specific antipneumococcus serum decreases the mortality, shortens the course of the disease, and lessens the frequency of complications.

SELECTION OF CASES

Our procedure in finding the answer to these three questions was to type as soon as possible after admission, each case which showed signs of pneumonia. The mere fact that we typed a case did not mean that it was used in the study. We included a case in our series only if by the time the type of pneumococcus was reported, the patient still had pneumonia with fever above 100°, and was not moribund. When the report of the pneumococcus type came back after the patient had died, the cases were not included as controls because we had no choice of using them as controls or serum-treated cases. This lack of choice compelled us to eliminate patients who recovered before the time the type report was obtained. Since it would have been unnecessary to give the serum to these cases at the time when the pneumococcus type was obtained, we could not in fairness use them as controls. If the pneumococcus type was one for which we had no serum, the case was placed in a separate category. If the pneumococcus type proved to be one for which serum was available, we made the case a control or serum-treated case, trying to have equal numbers in each group of each pneumococcus type. As far as it was possible, we also tried to match the cases according to age and severity of disease. Altogether

From the Fifth Avenue Hospital, New York City, (Director of Pediatrics, Dr. Frederick Bartlett), and from the Research Laboratories, Department of Health (Director William H. Park.)

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we attempted to type 131 cases. Only seventy-six are used in our serum study. The reasons for not including the remaining fifty-five cases are given in Table I.

TABLE I

REASONS FOR EXCLUDING 55 CASES

REASON	TOTAL NO.	DIED	
No pneumococci found	16	2	12%
Child died before report of the type was received	3	3	14%
Child had no fever at the time type was received	18	–	
Pneumococcus meningitis	1	1	100%
Pneumococcus peritonitis	1	–	
Pleural effusion at admission	5	–	
Unresolved pneumonia	2	–	
Upper respiratory infection	5	–	
Pneumonia diagnosis was erroneous	4	–	
TOTAL	55	6	11%

If we considered as controls the patients who lost their fever and the patients who died by the time the type report came back, the control mortality would be 14 per cent. Whereas, as shown in Table V, if we count as controls only the patients who had neither died nor lost their fever by the time the pneumococcus type was reported to us, the control mortality is only 7 per cent for those which could have been treated with serum. This method of selecting suitable cases for study might explain why our results with pneumococcus serums seem to be less favorable than those reported by some other workers.

FREQUENCY OF PNEUMOCOCCUS TYPES

Table II shows the frequency of the different pneumococcus types in all the cases where types were obtained. It is interesting to note that the dominating types among children are XIV, XIX, I and VI. Two or more types occur in about one-fourth of the cases. The age of our children varied from two months to eleven years of age, which explains why the frequency of pneumococci, falling into different types, varied from the order most commonly found in pneumonia of adults.

Two-thirds of the cases were lobar pneumonia with a mortality of 3 per cent. The remaining third were bronchopneumonia with a mortality of 20 per cent. These are total figures including both serum-treated and nonserum-treated cases. The two cases with pneumococcus meningitis died. Types XVIII and XIX seem to be especially dangerous. Empyema, as a complication, occurred in 11 per cent of the pneumonia cases. Only one of the thirteen empyema cases followed bronchopneumonia.

TABLE II

FREQUENCY OF PNEUMOCOCCUS TYPES AMONG CHILDREN

TYPE	TOTAL NUMBER	PER CENT	EMPYEMA		LOBAR PNEUMONIA	LOBAR PNEUMONIA DEATHS		BRONCHOPNEUMONIA	BRONCHOPNEUMONIA DEATHS		PNEUMOCOCCUS MENINGITIS	PNEUMOCOCCUS MENGIT. DEATHS		PNEUMOCOCCUS PERITONITIS	PNEUMOCOCCUS PERITON. DEATHS	NO PNEUMONIA	NO PNEUMONIA DEATHS
I	10	9%	2	20%	10	-		-	-		-	-		-	-	-	-
II	1	1%	-		-	-		1	-		-	-		-	-	-	-
III	3	3%	1	33%	3	-		-	-		-	-		-	-	-	-
IV	5	4%	-		4	-		-	-		-	-		-	-	1	-
V	4	3%	1	25%	3	-		1	-		-	-		-	-	-	-
VI	7	6%	1	14%	4	-		1	-		-	-		-	-	2	-
VII	3	3%	-		2	-		1	-		-	-		-	-	-	-
IX	1	1%	-		-	-		1	-		-	-		-	-	-	-
X	3	3%	1	33%	3	-		-	-		-	-		-	-	-	-
XIII	2	2%	-		1	-		-	-		-	-		-	-	1	-
XIV	17	15%	3	18%	15	1	7%	2	-		-	-		-	-	-	-
XVIII	4	3%	-		2	-		2	2	100%	-	-		-	-	-	-
XIX	14	12%	1	7%	4	-		7	3	43%	1	1	100%	-	-	2	-
XX	2	2%	-		2	-		-	-		-	-		-	-	-	-
XXI	3	3%	-		2	-		1	-		-	-		-	-	-	-
XXIII	3	3%	-		-	-		2	-		1	1	100%	-	-	-	-
XXVI	1	1%	-		1	-		-	-		-	-		-	-	-	-
XXVIII	2	2%	-		2	-		-	-		-	-		-	-	-	-
XXX	2	2%	-		-	-		1	-		-	-		-	-	1	-
Mixed types	28	24%	3	11%	17	1	6%	10	1	10%	-	-		1	-	-	-
Totals	115		13	11%	75	2	3%	30	6	20%	2	2	100%	1	-	7	-

RESULTS OF PNEUMOCOCCUS TYPING FROM DIFFERENT MATERIALS

Our routine method to obtain the type of pneumococcus was to secure a laryngeal swab.* One hundred and thirty-one cases were typed in this way; 87 per cent giving positive pneumococcus findings. The time required for the laboratory to make the type report on the throat swab was from six hours to two days. Since the type of pneumococci which are present in the throat are not necessarily the ones which cause the lung pathology, we decided to make both lung suction and throat-swab examinations on a limited number of cases.

The lung suction consisted of making a puncture into the portion of the lung showing the most definite pathologic signs on physical or roentgen examination. For this purpose a 10 c.c. syringe was used, with a 6-inch, 20-gauge needle. Four to 5 c.c. of plasma broth were drawn into the syringe and all air expelled. The media was then forced through the needle until it was quite certain that the entire length of the needle was filled by the broth. The needle was then inserted into the chest wall in the manner of an ordinary thoracocentesis. The proper limit of insertion was ascertained by the sense of resistance to the needle when it entered the lung parenchyma and the needle was forced into the lung tissue. The piston of the syringe was then pulled out partially and the media drawn into the barrel. The needle was then withdrawn and the media expelled into the culture tube. The needle was rinsed by repeated suction and expulsion of broth into the culture tube. Novocaine anesthesia was used on older children.

Throat swabs and material from lung suction were obtained in twenty-eight cases. Only 17 per cent positive results were obtained by one lung suction, in contrast to 60 per cent of the cases giving positive results by the first throat swab. A second throat swab examination brought the percentage of positive findings up to 96 per cent. We did not find the lung suction a quicker method because the average time needed for the laboratory to report on a lung suction was 1.7 days while only 1.4 days were required for the reporting of a throat swab. Twenty-four of the twenty-eight patients used for lung suctions had lobar pneumonia in which the place of pathology could be fairly easily determined. We had no complications such as pneumothorax or atelectasis from lung suction. Empyema, as a complication, occurred in 10 per cent of the cases which had lung puncture. As the frequency of empyema in our total group was 11 per cent we do not think that lung suction increased the frequency of empyema among our cases. Of the five cases with positive results for pneumococci, four showed the same one or two types as were found by the

*The swab was obtained with an ordinary applicator by attempting to reach the larynx and getting the child to cough up some of the sputum on the applicator. The swab was then placed in a culture tube of broth.

throat swab. One case showed Type III by swab and Type I by lung suction. As a whole, we do not see a sufficient advantage in using lung suction routinely instead of the throat swab for the determination of the pneumococcus type.

From sixty-five cases, one or more blood cultures were taken. Only four (6 per cent) showed positive results. In two of the four cases the type in the blood corresponded with the type in the throat. In one of the cases no throat swab was obtained, and in the fourth case the throat swab showed Type XIX and the blood, culture Type I pneumococci. One case had confluent bronchopneumonia, the other pneumococcus meningitis. Both were fatal. The third patient with lobar pneumonia, and the fourth with pneumococcus peritonitis recovered.

We had the opportunity to type the pus of ten cases of empyema. Six were positive, and of these, five corresponded with the type of pneumococci obtained by throat swabs while the sixth did not.

We studied the urine of five cases for precipitins. All five corresponded in type with the pneumococcus occurring in the throat. However, other types were also precipitated, which confused the results.

Table III gives the summary of the above described typings of different materials. We must remember in making comparisons that only one examination per case was done in almost every instance except in case of throat-swab examinations where swab taking was repeated several times until the type could be ascertained. However, 75 per cent of the cases were typed from the first throat specimen.

TABLE III

PNEUMOCOCCUS TYPING FROM DIFFERENT MATERIALS

MATERIAL USED FOR TYPING	TOTAL NUMBER	TYPE OBTAINED	CORRESPONDENCE WITH THROAT SWAB	REMARKS
Throat swab material	131	115 87%		
Lung suction material	28	5 17%	4 80%	
Blood	65	4 6%	2 67%	For one case no throat swab was obtained
Pus from empyema	10	6 60%	5 83%	
Urine	5	5 100%	5 100%	

PNEUMOCOCCUS SERUM TREATMENT OF PNEUMONIA IN CHILDREN

Serum was given intramuscularly or intravenously after skin and conjunctival tests for sensitivity were done. Where the sensitivity tests were found to be positive, the patients were first given small doses of serum in an attempt to desensitize. The dosage was increased as the sensitivity was overcome.

It was our intention to give approximately 1,000 units per pound of body weight per day to children over the age of two years, and about 2,000 units per pound per day to children under this age. This purpose could not always be adhered to as the titer of our serum varied—and with serum of low titer the dose of serum required became an impracticably large volume. In other cases the dose had to be diminished because of sensitivity.

The total dose for the twenty-four hours was divided into from three to four parts and given at intervals of from six to eight hours. The gluteal muscles were the area of choice for intramuscular injection, and the cubital or jugular veins or the longitudinal cerebral sinus for intravenous injections.

In order to compare the results in the serum-treated and control cases, we devised a scoring system for evaluating the severity of the cases before serum treatment was started, or before the case was put into the control groups. In this way, cases of similar age, color, bacteriological type, nutrition and complicating factors could be compared by score. The system is shown with the ratings given to the various findings in Table IV.

TABLE IV

RATINGS FOR PNEUMONIA STUDY

MAXIMUM SCORE 100, REPRESENTING THE WELL CHILD

	Deduct	Remarks
1. Cardiorespiratory System		25
Cyanosis	5 – 10	(Respirations 10-20 over normal 5)
Dyspnea	5 – 10	(Respirations more than 20 normal 10)
Pulse rate	5 – 10	(Pulse rate 20-40 over normal for age 5)
Pleurisy	5	(Pulse rate more than 40 over normal 10)
2. Gastrointestinal System		25
Diarrhea	5 – 10	
Vomiting	5 – 10	
Distention	5 – 10	
3. Evidences of Toxicity		20
Bacteremia	10 – 20	(Less than 5 colonies 10)
		(Over 5 colonies 20)
W.C.B.	5	(W.B.C. below 10,000 or above 35,000 5)
Marked enlargement of liver	5	
Temperature	5 – 10	(Temperature above 105° or below 98°)
4. Nervous System		15
Irritability, sleeplessness or delirium	5	
Meningismus	5	
Convulsions	5 – 10	
Apathy	5	
Coma	10	
5. Constitutional Factors		15
Organic heart lesions	5 – 10	
Severe malnutrition	5 – 10	
Active severe rickets	10 – 15	
R.B.C.	5	(Red blood cells below 4,000,000 or Hgb. below 60%—5)

TABLE V

SUMMARY OF PNEUMONIA SERUM TREATMENT STUDY

	TOTAL NUMBER	NUMBER OF DEATHS	DEATHS	AVERAGE DURATION	AVERAGE AGE	COMPLICATIONS	LOBAR PNEUMONIA	AVERAGE SCORE	COMPLICATIONS	MIXED TYPES
Controls with types to which no serum is available.	16	1 bronchopneumonia	6%	9 days	1.9 yr.	4 otitis med.	75%	80	25%	18%
Controls with types to which serum is available.	28	2 bronchopneumonia	7%	10 days	2.8 yr.	5 otitis med. 1 pleurisy 1 empyema 1 alim. intox.	64%	78	28%	32%
Intramuscularly serum treated cases.	17	1 lobar pneumonia	6%	9 days	3.6 yr.	3 otitis med. 2 empyema	76%	76	29%	29%
Intravenously serum treated cases.	15	1 lobar pneumonia 1 bronchopneumonia	13%	8 days	3.1 yr.	1 otitis med. 3 empyema	86%	75	26%	13%
All serum treated cases.	32	2 lobar pneumonia 1 bronchopneumonia	9%	8½ days	3.3 yr.	4 otitis med. 5 empyema	81%	75	28%	22%
Total number of treated and nontreated cases.	76	2 lobar pneumonia 4 bronchopenumonia	8%	9 days	2.8 yr.	13 otitis med. 1 pleurisy 6 empyema 1 alim. intox.	76%	77	28%	25%

Remarks: At present antipneumococcus serums are available to the following types: I, II, III, IV, V, VI, VII, VIII, IX, XIV, XV, XVIII, XIX, XXII.

TABLE VI

PNEUMONIA SERUM TREATMENT STUDY

TYPE	CONTROLS				INTRAMUSCULARLY TREATED CASES				INTRAVENOUSLY TREATED CASES			
	TOTALS	DIED	DURAT.	COMP.	TOTALS	DIED	DURAT.	COMP.	TOTALS	DIED	DURAT.	COMP.
I	1 – 0	0	10	0	3 – 0	0	9	1 empyema	4 – 0	0	7	1 empyema
II	1 – 0	0		1 otitis								
III	2 – 0	0	7	0					1 – 0	0		1 empyema
IV	1 – 0	0	5	0					1 – 0	0	11	0
V					1 – 1	0	10	1 otitis empyema	1 – 0	0	7	0
VI	1 – 1	0	9	0					2 – 0		9	1 empyema
VII					2 – 1	0	9	0				
VIII												
IX					0 – 1	0		0				
XIV	4 – 2	0	10	1 pleurisy 1 otitis media, purulenta, alim. intox.	2 – 0		10	0	3 – 0	1 lobar pneumonia	8	1 otitis
XV												
XVIII	1 – 0	0	8	0	1 – 0	0		1 otitis				
XIX	2 – 3	2 broncho-pneumonia	10	3 otitis					0 – 1	1 broncho-pneumonia		0
XXII				1 alim intox.								
Mixed types	5 – 4	0	11	1 empyema	4 – 1	1 lobar pneumonia	9	1 empyema 1 otitis	1 – 1	0	7	0
No serums	12 – 4	1 broncho-pneumonia	9	4 otitis								
Totals	30 – 14	3 broncho-pneumonia			13 – 4	1 lobar pneumonia			13 – 2	1 lobar pneumonia 1 broncho-pneumonia		

Remarks—First figure in totals, lobar pneumonia.
Last figure in totals, bronchopneumonia.

During the first year of our study we administered the antipneumococcus serum intramuscularly. As our results were not encouraging, during the second year we chose the intravenous method. As shown in Table V, the results with the intravenous injections were as indecisive as with the intramuscular method. The mortality rate was not lower in the serum-treated group than in the controls. There was a slightly shorter duration in the serum-treated group—a nine-day average in the intramuscularly and an eight-day average in the intravenously treated group against a ten-day average among the controls. The frequency of complications was alike in practically all groups. In order to find if any special reason existed why the serum-treated cases did not do better, they were studied from different points of view and compared with the controls of similar pneumococcus types. We know that the mortality rate of bronchopneumonia is greater than the death rate of lobar pneumonia and that younger children have a greater mortality rate than older ones. Also, if more than one pneumococcus type is found in a case, the serum treatment is more difficult, since we do not know which type caused the disease, and serum may not be available for more than one type. Finally, the prognosis is worse if the child is more sick and toxic clinically. One can see from Table V that the serum-treated cases had no apparent handicap from any of these factors. Lobar pneumonia was more frequent among these patients; they were on the average older; they had somewhat less frequently mixed types of pneumococci; and as judged by our scoring system they were not more sick when selected for treatment than were the controls. Therefore, the apparent failure of serum treatment might be due to the small number of cases upon which it was tried.

In Table VI the seventy-six cases are arranged according to types. The mortality for bronchopneumonia is considerably higher than the death rate for lobar pneumonia. Type XIX seems to be particularly dangerous.

Table VII also shows the deaths among the seventy-six cases tabulated above according to age and type of pneumonia.

Table VIII shows the details of serum treatment. We note that the interval between injections was nine and one-half hours in the intramuscularly and eight and one-half hours in the intravenously treated cases. In both groups treatment was started, on the average, between the fifth and sixth day of the disease. Thirty-three per cent of the intravenously treated cases showed mild signs of serum shock; one of them died. As death occurred one hour after the administration of serum, it is not certain whether it was a serum death. Intramuscularly treated cases had no signs of shock. A thermal reaction was noted in 17 per cent of the intramuscular and 26 per cent of the intravenous

TABLE VII

LOBAR AND BRONCHOPNEUMONIA CASES TABULATED BY AGE

TYPE OF CASES	ALL CASES ALL AGES		LOBAR PNEUMONIAS LESS THAN TWO YEARS OF AGE		LOBAR PNEUMONIAS MORE THAN TWO YEARS OF AGE		BRONCHO-PNEUMONIAS LESS THAN TWO YEARS OF AGE		BRONCHO-PNEUMONIAS MORE THAN TWO YEARS OF AGE		ALL PNEUMONIAS LESS THAN TWO YEARS OF AGE		ALL PNEUMONIAS MORE THAN TWO YEARS OF AGE	
	TOTAL	DEATHS	TOTAL	DEATHS	TOTAL	DEATHS	TOTAL	DEATHS	TOTAL	DEATHS	TOTAL	DEATHS	TOTAL	DEATHS
Controls with types for which no serum is available	16	1 6%	5	–	4	–	5	–	2	1	10	–	6	1
Controls with types for which serum is available	28	2 7%	8	–	9	–	9	2	2	–	17	2	11	–
Intramuscularly serum treated cases	17	1 6%	5	–	7	1	4	–	1	–	9	–	8	1
Intravenously serum treated cases	15	2 13%	5	1	9	–	1	1	–	–	6	2	9	–
All serum treated cases	32	3 9%	10	1	16	1	5	1	1	–	15	2	17	1
All pneumonia cases	76	6 8%	23	1 4%	29	1 3%	19	3 15%	5	1 20%	42	4 9%	34	2 6%

TABLE VIII

SERUM TREATED CASES

TYPE OF CASE	TOTAL NO. OF CASES	AVERAGE TOTAL NO. OF UNITS	AVERAGE INTERVAL IN HOURS BETWEEN INJECTIONS	AVERAGE NO. OF INJECTIONS	AVERAGE AMT. OF SERUM GIVEN FIRST DAY IN UNITS	AVERAGE AMT. OF SERUM GIVEN SECOND DAY IN UNITS	AVERAGE UNITS PER POUND PER 24 HOURS	AVERAGE DAY OF ILLNESS WHEN FIRST TREATED	SHOCK	THERMAL REACTION	CHILLS
Intramuscularly treated cases	17	95,666	9½	7	42,294	32,907 13 cases	1,518	5.7	0	17%	5.8%
Intravenously treated cases	15	37,133	8½	4*	21,815	14,666 9 cases	947	5.8	33% 1 death	26%	40.0%

*Four cases received only one injection.

group. Chills were observed in 5.8 per cent of the intramuscularly and in 40 per cent of the intravenously treated cases. As a whole the intravenous serum administration seemed to be a more severe and less comfortable method of treatment than the intramuscular route.

We treated seven Type I pneumococcus pneumonia cases, all of which recovered in a shorter average time than did the one untreated case which was kept as a control.

CONCLUSIONS

1. The most frequent pneumococcus types among children were XIV, XIX, I, and VI. Types XIV and I were likely to cause lobar pneumonia, whereas type XIX is most commonly found in bronchopneumonia.

2. The mortality from lobar pneumonia was 3.8 per cent; the death rate of bronchopneumonia 16.6 per cent in the series studied.

3. The average duration of pneumonia without serum treatment was ten days. If serum was given intramuscularly, the time was decreased to nine days; and when the serum was given intravenously, the length of disease was eight days.

4. Statistically there is no evidence that the serum treatment decreased the death rate. The number of our cases in the different types was too small to permit us to expect such evidence, and furthermore, the cases were obtained in late stages of the disease. Many more cases must be treated before we can be ready for a final decision in regard to the value of serum treatment. Analyzing the value of serum treatment on the different pneumococcus types, we find that Type I pneumonia seems to respond best to the specific treatment. As the serum has proved its value in lobar pneumonia in adults, it is somewhat significant that all seven cases of this type recovered in our series.

5. The multiplicity of pneumococcus types, the difficulty in identifying the type, the difficulty in obtaining potent serums for a variety of types, the necessity of the administration of serum at an early stage of the pneumonia, and finally, the careful attempt to avoid serum sickness and serum shock makes this research a difficult and time-consuming piece of work. It is evident that potent serum for at least the dominant types must be provided, and that many more cases must be treated before a final conclusion can be reached as to the practical value of the serums in the pneumonias due to the different types of pneumococci. To obtain this knowledge it will be necessary to utilize the children's services in a number of hospitals and the help of sufficient bacteriologists.

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CALCINOSIS UNIVERSALIS AND DERMATOMYOSITIS

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ABERRANT deposition of calcium in the various tissues and organs has been noted for many years and described by a large number of authors. There are apparently three main divisions under which this type of disturbance is seen.

Progressive Myositis Ossificans.—Munchmeyer[1] reported one case of his own and twelve from the literature in 1869. Helferich[2] in 1879 called attention to the prevalence of microdactyly and absence of a phalanx of the great toe in 75 per cent of his cases, which were similar to those of Munchmeyer. This type is apparently a distinct entity from the other two, inasmuch as the presence of congenital defects in such a large percentage of his cases would tend to prove an inherent deviation of calcium metabolism irrespective of other causative factors.

Metastatic Calcinosis.—This type is peculiar in that calcium deposits are found in the heart, lungs, kidneys and other organs while the muscles, fasciae and subcutaneous tissues are usually unaffected. With this condition there is usually a hypercalcemia and for that reason it is thought to be endocrine in origin and associated with some dysfunction of the parathyroids.

Calcinosis Universalis.—This third type, the one with which we are concerned in this paper, is characterized by calcium deposits in the tendons, fasciae and subcutaneous tissues without history of trauma, congenital defects, or hypercalcemia.

The first authentic case of this group was described in 1878 by Weber,[3] who considered it a form of gout. Since then, the condition has been the subject of a great deal of discussion as to etiology, pathology and therapy.

Durham[4] in a very excellent publication has reported a case associated with scleroderma and has reviewed the literature up to 1928. Since then, a number of cases have been reported.

Barr[5] describes calcinosis as a condition found with scleroderma and considers that it might possibly be due to deposition of calcium in dead or dying tissue and states the belief that most cases of abnormal calcification depend upon diminished blood supply and that they are preceded by changes resembling hyalinization.

Langmead[6] believes that scleroderma, dermatomyositis, calcinosis and myositis fibrosa are all related, that scleroderma and dermatomyositis are

almost inseparable and that universal calcinosis is probably a subsequent development.

Aisenberg[7] reports a case following soon after a malarial attack and believed it due to changes in calcium metabolism following injury to the parathyroids by the malaria.

Weil and Weismann-Netter[8] believe that the gouty diathesis is in part responsible for the development of the condition.

Moggi[9] considered his case to be due to excessive cholesterinemia due to prolonged exposure to the sun, the subject being inherently hypercholesterinemic. He warns that this etiology cannot be ascribed to all cases.

Weissenbach, Basch and Basch[10] believe that endocrine dysfunction may play a part but that tissue injury is the important factor. They observed circulatory injury with capillary disorder in all cases, leading to degeneration of connective tissue with secondary sclerosis.

Scholz[11] showed that the calcium deposits are not limited to areas under sclerosed skin but may be under apparently normal skin. He believes it dystrophic and metastatic.

Weissenbach, Francon and Robert[12] presented a case of subcutaneous calcification in which there was a family history of a marked tendency to calcium deposition and believes there is an endocrine background with local irritation in his case.

Von Bernuth[13] reported no calcium metabolic disturbance. He believes it is dependent on primary disease of the connective tissue, which may be congenital or endocrine in origin.

Bauer, Marble and Bennett[14] conducted extensive metabolic studies on the case of Wilens and Derby[15] and came to the conclusion that the condition was the result of a disturbed calcium metabolism.

The case herewith reported is presented in detail to show the development of the condition from the time of its inception to the development of calcification some two years later. It is fortunate that in the early stages the patient was confined in Harper Hospital, Detroit, and the University Hospital, Ann Arbor, where his case was carefully studied, the staffs of which we are indebted to for the use of their histories of the patient's stay in each institution.

CASE REPORT

The patient, a nine-year-old boy, was seen on June 1, 1932, complaining of stiffness of the joints with subcutaneous nodules scattered over the body.

Past History.—He had chickenpox in his third year and was circumcized in his fourth year; pertussis in 1928; pneumonia in 1928; tonsillectomy and adenoidectomy in 1928; measles in May, 1929.

Birth History.—Full-term normal noninstrumental delivery. Birth weight 9 pounds 8 ounces.

Family History.—Father and mother are living and well. No history of any condition simulating that of the patient.

History of present illness.—The mother states that in March, 1928, while in Florida he contracted pertussis, which lasted through April, May, and June. In June he was suddenly taken acutely ill with high fever and severe pains, which were apparently muscular. These pains were at first confined to the arms and legs, but gradually spread to all parts of the body although the arms and legs continued to be most affected, possibly because of the more frequent attempt to use them. There was at no time any swelling of the joints. Several days after the onset of the attack it was noticed that opening the mouth was painful and restricted and that there was some swelling of the face. During this acute period the pain was exquisite; the child could not be touched anywhere without screaming. This acute stage lasted for four or five days after which the temperature subsided and the tenderness decreased. However, there began a gradual progressive restriction and weakness of muscular movement. This became so severe that on December 5 he was admitted to Harper Hospital for study. In the interim between the acute attack and his admission to the hospital, the tonsils had been removed, which procedure was followed by pneumonia.

A résumé of his history at Harper Hospital is as follows:

"At first movement was not impaired. Later there was some inability to flex arms and legs. At the present time he walks on his toes and is unable to rise when he falls down, which is frequent. He cannot walk up or down stairs and must be carried most of the time. When he eats, he cannot bring his arm up to his mouth; he must move the head forward to meet the hand. He sits on the edge of the chair and is unable to sit up straight.

"Patient is well developed and well nourished. The cheeks seem somewhat puffed out and edematous; the eyelids are swollen. He does not appear acutely ill but is unable to sit up in bed. There is no muscular atrophy in the extremities. There is questionable hypothenar atrophy. The fingers are semiflexed, and he is unable to extend them normally. There is limitation of abduction in both arms. The legs are kept in semiflexed position and the Achilles tendons are contracted. Palmar flexion is present. He is unable to place foot at right angle to leg, and he is unable to flex leg on thigh or thigh on abdomen. This is bilateral. There are no sensory changes."

Laboratory Findings.—Hemoglobin, 85; R.B.C., 4,300,000; W.B.C., 12,000; polymorphonuclears, 65 per cent; lymphocytes, 27 per cent; monocytes, 3 per cent; eosinophiles, 5. Urine was negative in all respects. N.P.N., 27.3; sugar, 0.066 mgm.; Wassermann, negative; gold chloride 000,000,000; throat culture, staphylococcus.

The last progress note, January 5, 1929: "In general appearance the boy has not improved. He is docile and without spirit. His lips are a bluish color, and his skin has a pale bluish sheen. The general muscle tone is less. There is coordination in the movements of the body, but the grip and power of the upper extremities is reduced. Reflexes here are absent. There is a marked weakness in the lower extremities, almost to total paralysis with a mild contracture of the knee joint and slight toe slope. Here also reflexes are absent. Skin reflexes, subcutaneous and cremasteric are active. There is no Babinski reflex. Sense of motion and position is undisturbed. There are no sensory changes in the body."

He was discharged January 17, without diagnosis, and referred, for further study, to University Hospital, Ann Arbor, where he was admitted January 28, 1929. A résumé of the University Hospital records is as follows:

"Examination revealed generalized muscular weakness, but no paralysis was demonstrable. There were bilateral equinus deformities and bilateral flexion deformities of the hip. The only obtainable reflexes were the Achilles. The patient was given a complete electromuscular examination, and the muscles responded in the

normal way to the galvanic and faradic current. The entire dorsal and lumbar spine and pelvis were examined by the x-ray department with negative results. X-ray examination of entire lower extremities was negative, as were both elbows, wrists, and forearms. The patient ran 100° F. temperature during entire stay in hospital. The Kahn test was negative and the W.B.C., 6,600 with 75 per cent hemoglobin. No smear was made. The urine was negative.

"Patient was given physiotherapy in form of ultraviolet light, bakes, massage and active exercise in an attempt to correct his deformities and to increase the muscular system. On May 9, the patient was manipulated and the deformities corrected, following which physiotherapy was again started. He was discharged May 6, 1929. Patient was last seen in the clinic August 20, 1930, at which time the following note was made: 'Patient returns walking without pain and with marked improvement in all joints.'

"A diagnosis of residual poliomyelitis was made but the Orthopedic Department never felt this was the true state of affairs."

Fig. 1.—Appearance of nodules in buttocks region.

After his discharge from the hospital, there ensued several months during which he gradually learned to walk again although the act was accompanied by a good deal of pain.

He returned to Florida in the summer of 1930 and has gradually improved, and, although there was still a marked divergence from the normal in all of his motor actions, he was able to take care of himself, swim, throw a ball and do a little dancing act. It was still somewhat difficult for him to get up from a prone position.

The nodules first made their appearance in May, 1931, the mother stating that she noticed them shortly after Spanish fly plasters had been applied to the boy's spine by a physician. She noticed "lumps" all over him, especially in the region of the buttocks. Since their first appearance, they have grown much larger and harder though there has been very little progress in either direction during the last six months. The mother stated that there has been a marked improvement in his motor activities since their appearance.

Physical examination.—Examination revealed a well-developed and well-nourished white male weighing 49 pounds. Stripped, he had a peculiar appearance that may best be described as "tightness," as though there were lacking the normal body

elasticity. The lower eyelids had a reddened appearance as though he had been rubbing them. This was persistent. He had also over the extensor surfaces of the hands a red annular rash, which came and went. There was a broken down area on the right elbow which the parents stated had been there a year, alternately breaking down and clearing up.

There were a great number of nodules scattered over different parts of the body with a decided tendency toward clumping in certain areas. This was especially marked in the axillary region, the buttocks, and the anterior surface of the neck.

Fig. 2.—Roentgenogram of pelvic region showing extensive calcium deposits.

Their location in regard to depth also varied, some of them seeming to lie directly under, though not attached to, the skin, others lying deep in the subcutaneous tissues, and still others along the tendons. On the other hand, there were areas that seemed to be entirely free from nodule formation, in particular, over the pectoral area and the back. These nodules varied considerably in their consistency, some seeming tough and fibrous while others were bony in their hardness.

Motor activity: There was no muscular atrophy. There was an inability to flex the hand on the forearm and to extend the forearm normally in relation to the arm. The body could be bent only 45 degrees on the hips, and there was a mild

lordosis. The fingers were stiff and could not be extended normally although the grip was of average strength. There was no equinus deformity at this time. The child carried himself in a rather "poker back" posture. There was marked restriction in opening the mouth. There were no deformities of the fingers or toes aside from the sclerodactylia. There were no sensory disturbances.

Laboratory examination.—Kahn test was negative; urine, negative in all respects. Blood count did not diverge from the normal. Stool was negative for ova and parasites.

Fig. 3.—Roentgenogram of left leg.

X-rays of the shoulders, hips, neck, and pelvic region showed refractile deposits in the locations mentioned on physical examination.

Permission was granted for biopsy, and one of the smaller and more superficial nodules was removed from the buttocks. On removal, this nodule seemed to consist of a fibrous matrix, embedded in which was a hard, bonelike substance which would not crumble between the fingers. The pathologic report was as follows: "Microscopic section through the softer portions of the nodule show no evidence of malignancy. Microscopically there is a predominance of rather dense connective

tissue associated with a few round cells and plasma cells, a considerable amount of fat, and also a large number of amyloid bodies, many of which have undergone calcification."

An attempt made to keep this child on a ketogenic diet as advocated by Kennedy[16] met with no cooperation and was abandoned as was the ammonium chloride route to ketosis as used by Skossogorenko[17] for the same reason. This condition remained

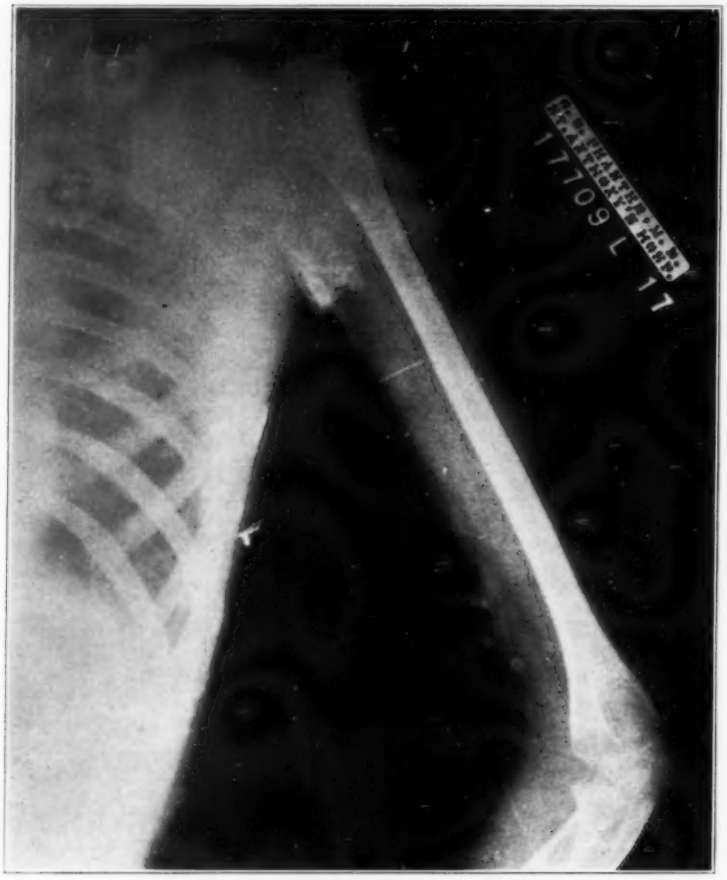

Fig. 4.—Roentgenogram showing calcium deposits in axillary region.

unchanged until January, 1933, when several of these areas became infected, broke down and exuded large amounts of pus, which contained chalky material, and left behind sinuses that healed with difficulty. He was ill with high fever and a good deal of pain for a period of about two months. Following this he was treated by means of medicine internally and ultraviolet light. On June 1, 1933, he was brought back to my office and showed marked improvement, many of the larger areas having disappeared and his motor activity correspondingly increased. Hein[18] has recently reported a case that over a period of several years with ultraviolet treatment has

shown marked improvement. On the other hand, a prolonged illness with fever perhaps produced a sufficient ketosis to influence absorption of calcium from these areas.

DISCUSSION

The similarity between this case and others reported may be shown in a brief review of a few of these cases.

Craig and Lyall's[19] case began suddenly with pain, fever and swelling in February, 1926, followed by prolonged muscular weakness and the development of calcified nodules in March, 1927.

Wilens' and Derby's patient, two and one-half years old, showed muscular weakness, dropped to his knees, and was unsteady for six months previous to the onset of calcification.

Skossogorenko's patient had an acute infection with high fever in 1922. Five months later he had edema of both extremities and lost use of them. This lasted for three years, at the end of which time he resumed some use of his limbs; the edema disappeared, and calcified nodules made their appearance.

Morse's[20] patient was sick for a week with influenza, a month later fell from a chair, and soon after stopped walking. The calcium nodules were discovered some months later.

Kennedy noted instability and difficulty in walking for two years preceding the onset of calcium deposits.

While all of the cases reported do not show so clear cut a sequence of events, yet there are certainly enough of them to lead us to the belief that, at least with children, the essential features are an acute illness followed by muscular weakness, which in a varying length of time is followed by calcium deposition. This idea, however, is not new although there still remains the question as to whether the preceding condition is one of dermatomyositis or scleroderma. These two entities are so similar to each other that there is often extreme difficulty in differentiating them. Allan[21] considered the two identical, while Langmead,[6] Cullinan,[22] and Steinfield,[23] though doubting their identity, admit that there is a very close relationship between the two. Steinfield's case of dermatomyositis showed sclerodermic changes, and he states that this is frequently the case.

The present case, however, coincides so thoroughly with the excellent description of dermatomyositis as given by Karelitz and Welt[24] and differs so from the usual description of scleroderma that we are forced to the conclusion, unless the two conditions are one and the same, that in this instance there was a prevailing dermatomyositis.

As to the actual pathologic process involved, there remains a great deal to clear up.

The theory of endocrine origin seems untenable in that all of these cases have shown normal blood calcium figures and the one case that has

come to autopsy, that of Durham, has shown apparently normal parathyroids, both macroscopically and histologically.

That there is present a distorted calcium metabolism has been shown by Bauer, Marble and Bennett. On an inadequate calcium intake (0.286 grams per three-day period), their patient showed a positive calcium balance of 0.170 grams per three-day period. Two normal boys, aged nine and fourteen years, on the same inadequate intake showed a negative balance of 0.46 grams. This same imbalance was shown to be true of phosphorus. It is likely, however, that this change of balance is the result rather than the cause of the deposition of calcium. Besides, a theory of metabolic disorder would not account for the acute onset, the prolonged muscular weakness, and the duration of time between onset and calcium deposition, or for the unquestioned improvement in this patient with the appearance of the nodules.

Durham has made some very interesting observations regarding the capillaries in scleroderma. He noted enlargement of the capillaries with the venous ends distended like bulbs and with a sluggish flow of blood, and after adrenalin injection, almost complete stasis in the smaller capillaries and marked slowing in the larger. These observations seemed especially important in view of Hofmeister's[25] belief that as soon as a fluid loses its free carbonic acid, provided there is no increase in the velocity in the fluid flow or a higher protein content, a deposition of calcium phosphate can occur.

Hunter[26] believes the condition is similar to the deposition of calcium salts in tuberculous lesions or sclerosed heart valves, i.e., an end-result of fibrosis.

Pospelow[27] mentioned the affinity between elastic fibers and calcium salts and believes that deposits can occur in normal elastic tissue.

While all writers on this subject, with the exception of Morse, have been unable to find evidence of fat, elastic, or connective tissue injury after calcium has been deposited, it seems highly probable that this must have occurred either from direct bacterial or toxic action or through interference with the normal circulation to these areas. It is certainly conceivable that injury to these types of tissues, none of which possess any definite organ morphology, could not be readily detected after the acute condition has cleared. That injury to the circulation does take place with dermatomyositis has been shown by Bass and Denzer,[28] Batten[29] and by Karelitz and Welt, the latter in an exhaustive pathologic report on one of their cases noted "perivascular round cell infiltration, thickening of the vessel walls, and occasional obliteration of a vessel plus involvement of the musculature of the vessel."

The simplest and most tenable suggestion as to the pathogenesis of this condition would therefore seem to be a diffuse involvement of the sub-

cutaneous tissues by dermatomyositis, scleroderma, or a similar disease with a consequent alteration, either in the tissue itself or following indirectly a vascular injury, favoring the deposit of lime salts.

SUMMARY

A case of calcinosis universalis is reported with an attempt to trace its origin from a pre-existing condition which was apparently dermatomyositis.

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ACHONDROPLASIA IN A TWIN

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LITERATURE is replete with reports of cases of achondroplasia, but a thorough search fails to reveal a definite case in twins. Hutchinson[1] cites one case in twins, but the pictures are poor and show very few signs of achondroplasia.

Achondroplasia, the name given to this entity by Parrot[2] in 1890, has been referred to by many writers as fetal rickets, intrauterine rickets, and fetal cretinism. Kaufmann,[3] as a result of his pathologic studies in this disease, called it chondrodystrophia foetalis. It is a Mendelian character (dominant) and is characterized by dwarfism, with short stout limbs, body normal, though relatively long, and head hydrocephalic in appearance.

The etiology is still the subject of controversy and surmise. Some observers, De la Torre and Allende,[4] believe it to be hereditary and support their opinion by citing a case in which consanguinity was responsible. Thomson[5] asserts that it is due to a definite pathologic condition during uterine life. Wheeldon[6] observes that the changes in achondroplasia are probably due to the smallness of the amnion and that they are produced between the third and eighth weeks of intrauterine life. Durante[7] believes that it is due to a sclerosis of the zone of the endochondral ossification. Kaufmann[3] as a result of his many observations shows that there is a primary malformation of the epiphyseal cartilages and early cessation of endochondral bone formation.

The following report of a definite case in a twin is presented because of its interest and rarity in the literature:

Rosemary S., aged ten months, was brought to the Pediatric Clinic of Lebanon Hospital by her mother, who told us that she thought that this child "looked different than the other twin sister." Investigation revealed that this child was one of twins, both girls; that it was born at term; delivery had been normal; that the father was of normal height and had normal physical features; the mother of average height with normal physical features; both of average intelligence; that they were not related by blood; and that there was no similar child in either branch of the family for three generations back.

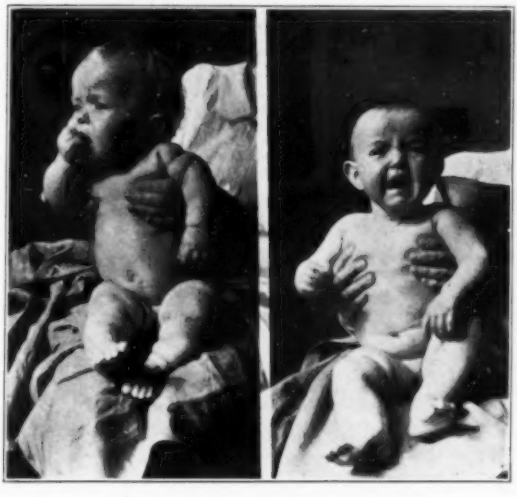
The history showed that the child had been bottle fed since birth and had always been well with the exception of diarrhea two months previously which lasted for several days.

From the Pediatric Division of the Lebanon Hospital Dispensary.

On examination we found an obese, well-nourished child ten months old, who could not sit up and who showed a general hypotonicity of the muscles and joints. The weight was 16½ pounds, and length 24 inches. The head was very large and hydrocephalic in appearance with very prominent frontal and occipital bulges. The circumference of the head was 18½ inches, and the anterior fontanel was 2¼ inches in diameter. The face showed heavy and broad features, with a short stubby nose depressed at the bridge. The mouth presented a high-vaulted palate.

Fig. 1.—The well-nourished achondroplastic twin with the typical facies and marked pads of fat on extremities.

Fig. 2.—Showing the large head, the short, stunted limbs and the disproportion between body and extremities.



A. *B.*

Fig. 3.—The twins side by side. *A.* The achondrocephalic twin. *B.* The normal twin. (Note the length of upper extremities and their relationship to the umbilicus.)

The neck showed no rigidity. There was no adenopathy or palpable enlargement of the thyroid. There was slight beading at the costocervical junction of the chest. Lungs and heart were normal. The abdomen was protuberant, the hips large and fleshy. A definite lumbar lordosis was present.

The extremities were short and stubby, markedly obese, with pads of fat hanging loosely over arms and legs. The forearms were larger than the arms, and the legs, longer than the thighs, were quite bowed. The arms when extended reached about to the level of the umbilicus. The hands were quite characteristic, the fingers being short, stubby, and fleshy, and of almost equal length—the so-called trident hand. The forearm measured 3¾ inches; the leg, 3¾ inches; anterosuperior spine to heel, 9 inches; tip of acromian to styloid of radius, 6¼ inches; episternal notch, to symphysis pubis 11½ inches. The disproportion between the body and the extremities was quite marked, and this was apparent when both twins were placed side by side.

The other twin, Elizabeth S., was normal in every respect, weighed 22 pounds and 9 ounces; length, 29 inches; she sat up well and had four teeth. The forearm measured 4½ inches; leg, 5¼ inches, circumference of head, 16¼ inches; and the anterior fontanel, 1¼ inches in diameter. This normal twin always cried and was tempestuous in nature, while its abnormal sister was generally good-natured and placid in disposition during all the examinations.

Radiologic examinations revealed no pathology in the bones of the skull. The posterior fontanel was closed; the anterior fontanel, open; and sella turcica normal. The left forearm disclosed a broadening and cup-shaped deformity of the distal end of the shaft of the radius and ulna, with fraying. The right forearm showed a broadening and irregularity of the distal end of the diaphysis of the radius and ulna. All the bones of the hands appeared shorter and broader than normal. There was an absence of distal epiphysis of tibia and fibula of both legs, with an irregularity and widening of the distal ends of the tibia and fibula. X-ray pictures of the skull and long bones of the normal twin failed to reveal any abnormality. The above described x-ray findings are generally found in achondroplasia, but are usually more marked. This patient was too young to show the synostosis of the nuclei of the vertebral arches, with the resulting flattening and narrowing of the vertebral canal.

COMMENT

This case illustrates all the features and characteristics of achondroplasia and is remarkable inasmuch as it occurred in a twin. It is difficult sometimes, in the early months of infancy, especially in a very obese child, to make a diagnosis of micromelia, the characteristic feature of achondroplasia. In this case the child was seen at ten months of age, and there was the added advantage of having it presented at the clinic with its normal twin. The general puffed or bloated appearance of the child with its unusually large head makes one think of cretinism. The short extremities, the disproportion between the trunk and the extremities and the x-ray findings leave no doubt as to the diagnosis of achondroplasia, as the accompanying photographs illustrate.

The interest in this case centers around the fact that it occurred in a twin. If we assume that these twins were of the uniovular type, the difference in the physical development, according to I. A. Abt,[8] may be assumed to have occurred as a result of an unequal division of the germ

plasm; or, as in some instances, the arrested development of bone in this condition may be accounted for as result of a poor blood supply to one twin, through a long and winding umbilical cord.

While many authors report no changes in the thyroid and no alteration in the physical appearance of these patients as a result of thyroid treatment, still it is not unreasonable to assume that the condition may be due to some endocrine gland disturbance. Wagner[9] seems to think that the condition is influenced by some prenatal deficiency. He is of the opinion that the modification of the growth of the bone may be caused by excessive gonad activity or by interaction of other endocrine glands. Abels[10] remarks that the condition is due to a disturbance in the internal secretory equilibrium, and he shows that some changes in the thyroid, abnormal development of the genitals, and overdeveloping of the muscular and digestive systems, indicating an abnormally increased productive stimulus, are often found.

While the endocrine theory has been set aside by many authors as not tenable, we believe with the increased knowledge of the functions of the active principles of the endocrine glands—the hormones and chalones—we shall be able to fathom the phenomenon of achondroplasia.

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Bronx Professional Building, 2021 Grand Concourse

THE EFFECT OF SMALL QUANTITIES OF BREAST MILK, LIVER EXTRACT, IRON AND COPPER, RESPECTIVELY AND IN COMBINATIONS, UPON THE IRON BALANCE OF ARTIFICIALLY FED INFANTS

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KRASNOGORSKY,[1] in making iron balance determinations on breast-fed and artificially fed infants, concluded that the iron compounds of breast milk are absorbed and retained to a considerably higher degree than those of goat's milk.

Langstein and Edelstein[2] declared Krasnogorsky's iron values were too high. Soxhlet[3] criticized the methods employed by Bahrdt and Edelstein[4] and Edelstein and Csonka[5] as being merely oxidation and reduction methods giving unreliable results. Langstein and Edelstein[6] discussed Soxhlet's attack on their methods and concluded that, fundamentally, Soxhlet obtained the very same results on the iron content of cow's milk used in the artificial feeding of infants, as they did some time before Soxhlet's publication. Although Langstein and Edelstein criticized Krasnogorsky's work, their data on breast-fed infants confirmed his conclusions.

In this work we have repeated and confirmed Krasnogorsky's iron balance observation on breast-fed infants and partially confirmed those on the artificially fed. The studies were extended to include the effect of liver extract, copper, iron (inorganic and organic), and different combinations of these substances upon the absorption of iron from the gastrointestinal tract of young artificially fed infants.

Five groups of infants were used, comprising a total of seventeen cases. The four artificially fed groups each consisted of three infants of approximately the same age. The data are charted as column graphs. Each column represents the average per day per infant obtained for the group. The red cell count is charted as millions per cubic millimeter. The hemoglobin is charted in grams of hemoglobin per 100 c.c. of blood.

The amount of iron intake per infant is the average number of milligrams of iron consumed in the formulas per day over the three-day stool collecting period.

From the St. Vincent's Infant and Maternity Hospital, the Otho S. A. Sprague Memorial Institute, and Department of Pathology, University of Chicago.

We wish to thank Armour and Company for the concentrated liver extract and iron used in this experiment and the grant for the quantitative iron determinations.

The iron balance is the result obtained by subtracting the average daily milligrams of iron in the stool from the average daily iron consumed per infant. When the iron in the stool is greater than the iron consumed in the diet, the balance is negative. If the iron in the stool is less than the iron consumed, the balance is positive.

Method.—The total three-day stools of each infant were pooled together, dried, ignited, and digested free of organic material in concentrated H_2SO_4 on the Kjeldahl shelf, hastening the oxidation by repeated additions of concentrated HNO_3. Known quantities of reagents were used and their iron content subtracted from the final determinations. The sulphuric acid digest was diluted to a known volume and an aliquot portion used for the quantitative iron determination. The iron was precipi-

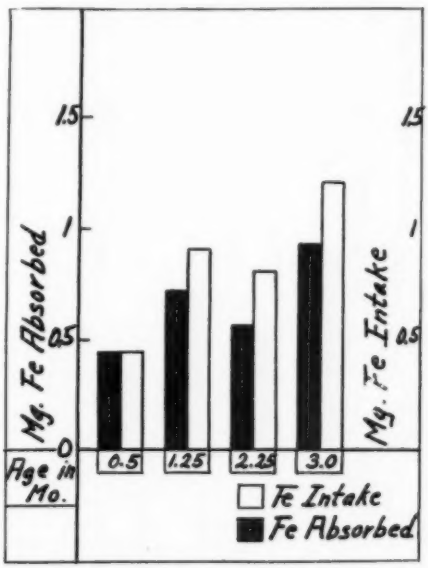

Chart 1.—The average iron balance of three breast-fed infants. The age of these infants was three weeks at the beginning of the experiment. The increase in iron intake was due to complement feedings.

tated from the solution by concentrated NH_4OH. The solution was heated to boiling, and $Fe_2(OH)_6$ filtered and washed with boiling water to avoid loss by solution of the $Fe_2(OH)_6$, which is slightly soluble in cold water. The washed precipitate of $Fe_2(OH)_6$ was dissolved on the filter paper with hot concentrated HCl, and the filter paper washed free of iron. The iron solution was made to volume, and a portion used for colorimetric iron determination using the method of Kennedy.[7]

Red cells were diluted in a calibrated pipette and counted on a Bureau of Standards government-certified, double-ruled Levy counting chamber.

The hemoglobin determinations were made with a Fleischl-Miescher hemoglobinometer. The blood was obtained from a freely bleeding heel stab wound. The counts were always made at about the same time after feeding.

Results.—The average iron balance of five breast-fed infants is shown in Chart 1. These infants varied in ages during the study from two

weeks to three months. The chart shows an average of 2, 5, 3, and 4 determinations from the ages of two weeks to three months, respectively. As the infants grew older they received complementary feedings, which were richer in iron than the human milk, so that the iron intake gradually increased from 0.44 mg. per day at two weeks to 1.4 mg. per day at three months. On this low iron intake, the infants absorbed a good

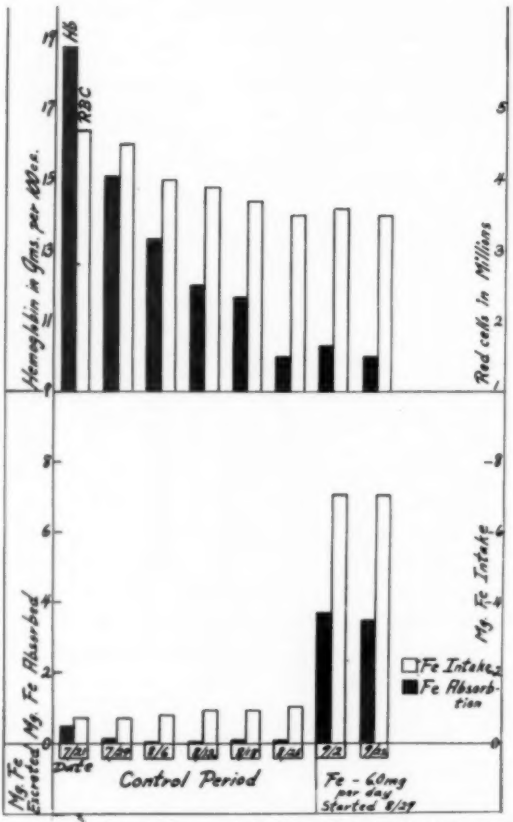

Chart 2.—The average iron balance of three artificially fed infants with approximately normal blood, averaging three weeks of age at the beginning of the experiment.

portion of iron ranging from 100 per cent early in the experiment to 78 per cent at the age of three months when the breast milk intake was about 6 ounces daily. Snelling[8] in a study on premature infants found an average daily positive iron balance of 0.10 mg.

The iron absorption from the gastrointestinal tract of three artificially fed infants whose blood was normal during the experiment is shown in Chart 2. The experiment was started when the infants were three weeks

old. Throughout the period, a small quantity of iron was absorbed. After the first week the amount of iron absorbed was of little significance when compared to that absorbed by the infants receiving the breast milk plus additional iron. These infants were fed 6 mg. of iron as iron ammonium citrate on and after August 29. Stool determinations made on September 2 and 22 showed a positive balance of 3.7 and 3.5 mg.

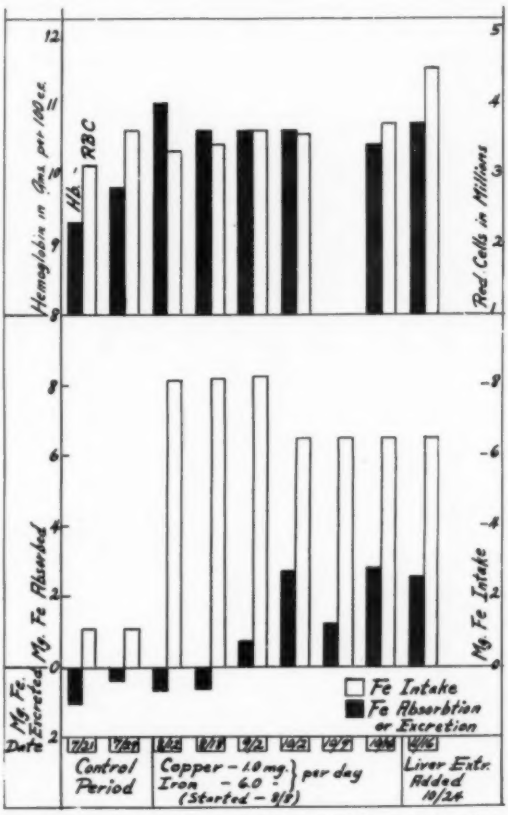

Chart 3.—The average iron balance of three slightly anemic, three-and-one-half-month-old infants who received copper and iron.

NOTE:—In graphs number 3-4-5, when the column is charted on the excreted side of the base line, the value charted indicates the quantity of iron found in the stool in excess of the intake of iron in the diet. This iron must have been derived from the body iron storage.

of iron. A little less than half of the iron consumed in the diet was absorbed and retained by the body.

Observations on the effect of copper and iron upon the iron balance of three slightly anemic, artificially fed infants were started at the age of three and a half months (Chart 3). During two periods of stool collection prior to the administration of copper and iron, the infants

showed a negative iron balance of 1.1 and 0.4 mg. During the first three weeks of administration of the iron and copper, a negative iron balance of 0.7 mg. and 0.6 mg. and a positive iron balance of 0.7 mg. were found, respectively. Following the administration of copper and iron, the hemoglobin maintained 0.8 gram increase even though a small quantity of iron was lost from the body storage during this period. These data demonstrate the mobilization of retained iron by copper administration, part of which was excreted by the intestines and part built into hemo-

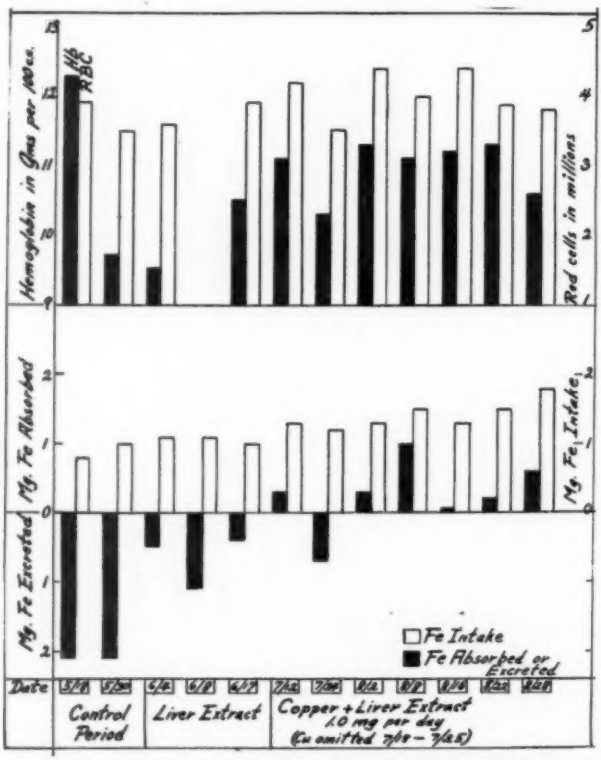

Chart 4.—The average iron balance of three slightly anemic infants (averaging 2.6 months of age) who received liver extract and copper.

globin. During the infants' fifth month the accompanying chart shows that an appreciable quantity of iron was absorbed from the gastrointestinal tract to support growth after the exhaustion of the retained iron. Liver extract was administered in addition to the iron during the infants' sixth month and was accompanied by an increase in red cells only.

Liver extract, and liver extract and copper, respectively, were fed to a group of three slightly anemic infants, whose average age was

two and six-tenths months; and average hemoglobin, 9.0 gm.; and red blood cells, 3.6 millions. (Chart 4.) The preliminary study made on the iron balance before the experiment started showed a negative iron balance of 2.1 mg. iron on May 18 and May 30, respectively. Because of the low red blood count, liver extract was started on June 3, at which time an average of 3.6 million cells and a 9.5 gm. hemoglobin was found. On June 17 the red blood cells had increased to 3.9 millions, and hemoglobin to 10.5 gm. The negative iron balance had decreased to 0.4 mg. One mg. of copper per day was started July 8. By July 12 the red blood

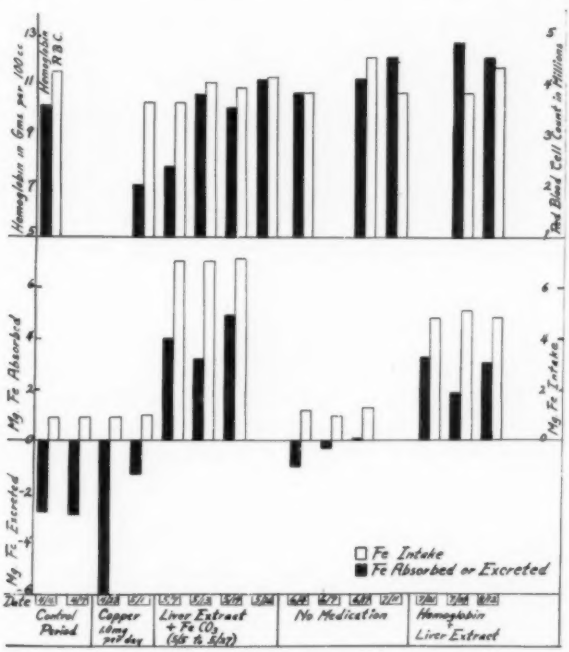

Chart 5.—The average iron balance of three anemic, artificially fed infants (averaging two months of age at the beginning of the experiment) who received copper, liver extract with hemoglobin.

count rose to 4.2 millions, and the iron balance became positive 0.3 mg. From July 18 to July 25 no copper was given. On July 24, six days after the suspension of copper, the red count and iron balance returned to about the same value as before the administration of copper. After August 2 the hemoglobin remained above 11 gm. and R.B.C. nearer 4 millions. By August 28 when the groups were over five and one-half months old, the red blood count and hemoglobin began to drop. Undoubtedly this was due to the low iron intake and the early iron loss with exhaustion of the iron storage. The increase of the tissues through growth of the infant requires more "function iron" than that absorbed

from the digestive tract so that at this stage the blood gives up its hemoglobin iron to the tissues for "function iron." This group later gained in the R.B.C. and hemoglobin when the iron was added. On November 5 the urine of two of the infants of this group was collected and found to contain 0.062 and 0.042 mg. of iron per 100 c.c., respectively. This accounts for 2½ per cent of the iron absorbed at this time. These infants were receiving 15 mg. and absorbing 12 mg.

Three anemic infants (Chart 5) were used for a study of the effect of copper, liver extract and inorganic iron ($FeCO_3$), and liver extract and organic iron (hemoglobin) upon the iron balance.

Stool collection was started when the group was two months of age. The hemoglobin at this time was 10 gm. and the R.B.C. 4.3 millions. There was a negative iron balance of 2.8 and 2.7 mg. on April 16 and 19, respectively. One mg. of copper daily was started on April 22. There was a negative iron balance of 6 mg. and 1.3 mg. on April 23 and May 1, respectively. On May 1 the hemoglobin was 7 gm. per 100 c.c. and the R.B.C. was 3.6 millions. Copper administration was stopped on May 3. Liver extract containing iron in solution was started on May 5, continuing through May 27, during which time the hemoglobin rose to 11 gm. and the R.B.C. to 4 millions. During this period the iron balance was positive, 4.0, 3.2, and 4.4 mg. daily on May 7, 13, and 19, respectively. No medication was administered from May 27 to July 18 during which time the iron balance gradually rose from negative 1.0 mg. to positive 0.1 mg. for determinations made on June 4, 7, and 17, respectively.

On July 18 iron was administered as hemoglobin with liver extract. The iron balance on July 21, 29, and August 12 was +3.3, +1.9, and +3.1 mg., respectively, or about one-half of the iron in the diet. The iron derived from the diet other than the hemoglobin was 1.0 mg. daily. This demonstrates that infants, six months old, receiving liver extract are capable of absorbing iron derived from hemoglobin. However, the hemoglobin as a source of iron was not well tolerated by the infants as it frequently produced diarrhea.

COMMENT

The mechanism of the production of anemia in infants and the effectiveness of various agents used therapeutically has excited great interest for many years. The significance of studies on iron balance as an index of the development of anemia and of the effectiveness of a therapeutic agent is apparent. In this investigation, the iron balance of five groups of infants was studied from a number of standpoints. First, the relationship of the type of feeding, human milk, human milk plus cow's milk, or cow's milk modifications was studied alone. Second, the effect of various therapeutic agents such as the additions of inorganic iron to the dietary, the effect of inorganic iron plus small amounts of

copper, the effect of liver extract alone, the effect of liver extract and iron, (a) as inorganic iron and (b) as organic iron in the form of hemoglobin were observed.

TYPE OF FEEDING AND IRON BALANCE

When the only source of iron in the dietary is from the milk, a striking difference in the amount utilized in breast-fed babies and those entirely artificially fed is observed. Krasnogorsky found the iron of breast milk was more available than that of goat's milk. As a result of our findings, the same statement may be made with regard to cow's milk. As the infants grew older, the principal source of the food was from complemental feedings of cow's milk modifications. Thus at the age of three months, these infants were receiving only 6 ounces of breast milk daily. The complemental feeding brought the iron intake up to over 1.25 mg. per day, most of which was absorbed. The addition of even relatively small amounts of breast milk appears to increase the availability of iron. This would seem to indicate some specific effect of breast milk upon the absorption of dietary iron. After breast milk was entirely discontinued, the iron balance soon became negative. One group of artificially fed infants, showing practically no anemia, had a low positive iron balance, which demonstrates that some infants do absorb the iron of cow's milk mixtures.

Kleinschmidt[9] called attention to the relationship of the development of anemia to the amount of cow's milk in the feeding. These authors felt there was some specific toxic substance in cow's milk responsible for the production of anemia and treated such cases by the withdrawal of practically all milk and the introduction of mixed feeding with large amounts of vegetables and fruits. The data we have demonstrate the relationship of iron balance to the production of anemia, and the change from a positive to a negative iron balance with the transition from human milk to artificial feeding with cow's milk mixtures. It seems likely that the development of anemia on artificial feeding with milk modifications, exclusively, is related to the lack of some quality of breast milk rather than to specific toxic effect of cow's milk.

ADDITIONS OF INORGANIC IRON TO THE DIET

In the group of artificially fed infants showing a low positive iron balance, iron and ammonium citrate was fed in dosages yielding 6 mg. of iron per day. The amount of iron absorbed by these infants before therapy was started was insignificant. After additional iron was fed, the balance became definitely positive with absorption of a little less than half the iron intake. When copper was added to inorganic iron and fed to a group of infants showing a negative iron balance during the control period, the balance continued negative for the first two weeks of the experiment. Following this, the amount of iron absorbed in-

creased appreciably. With the introduction of copper, a gain in hemoglobin was observed, which gain was maintained in spite of the negative balance. This may be interpreted as a demonstration of the effect of copper in mobilization of iron stores with utilization of a portion for hemoglobin synthesis and excretion of the remainder through the gastrointestinal tract. A second group fed copper alone in doses of 1 mg. per day showed a negative iron balance for a two-week period during which time the hemoglobin steadily fell until a value of 7 grams per 100 c.c. was obtained at the end of the two-week period. Thus an increased absorption of dietary iron with copper feeding was not observed.

EFFECT OF LIVER EXTRACT

Liver extract was fed to three groups. Group 3 received it as an addition to the copper and iron feeding at the end of the experiment. This group showed a good increase in red blood cells, an increase which was maintained after the experiment was discontinued, the hemoglobin remaining about normal. Group 4 received liver extract and showed a good increase in hemoglobin while the group was in negative balance. With the addition of copper to the liver extract, the balance became positive and further gain in blood appeared. The copper was discontinued for a week; and at the end of this period, the hemoglobin had dropped appreciably, and the iron balance again became negative. When copper was again introduced, the balance again became positive with a good gain in blood, which was maintained until the infants were close to six months of age when a drop again became manifest, probably the result of the exhaustion of iron stores. Group 5 was fed a combination of liver extract and iron carbonate after a preliminary period of copper feeding, during which the blood count dropped steadily and the iron balance remained negative. When liver extract and iron were substituted for the copper, the iron balance became positive and hemoglobin and R.B.C. steadily rose to normal levels. After a period without medication, this group was fed a combination of liver extract and hemoglobin, as a source of iron. The iron balance demonstrated absorption of the iron derived from hemoglobin. Lintzel[10, 11] in 1928 and 1930 was unable to demonstrate iron absorption in animals when hemoglobin only was used as a source of iron. The liver extract evidently contains some element which increases the absorption of inorganic or organic iron from the gastrointestinal tract of many anemic infants.

In a study of the effect of $FeCO_3$, liver extract, and the two combined, on the hemoglobin and red blood cells of artificially fed infants,[12] we showed that 30 per cent were benefited by the iron, about 50 per cent by liver extract alone, and 80 per cent by the two combined. The iron contained a trace of copper as did the liver extract. At first thought it would appear that the iron carbonate was absorbed and built into hemoglobin by the infants. This absorption of iron is shown in Chart 2. From the

infants who gained in hemoglobin from the liver extract, one can only conclude that the iron for the increased hemoglobin was derived from the iron retained after birth. This is demonstrated by the iron balance of Group 4, Chart 4, which shows an increase in hemoglobin even though there is a slight negative balance. The infants received 0.0002 mg. copper in the 15 c.c. of liver extract fed daily.

CONCLUSIONS

1. Nine out of twelve artificially fed infants studied showed negative iron balances, the more severe anemias having been present in the group which had a rather high negative balance.

2. A small quantity of breast milk greatly facilitated the absorption of iron from the gastrointestinal tract.

3. In the artificially fed infants studied, copper and iron showed no more effect on the iron balance than iron alone.

4. Liver extract and iron showed the most marked improvement in the iron balance of the artificially fed infants studied, whether the iron was derived from inorganic salts or from hemoglobin.

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CONSTIPATION IN BREAST-FED INFANTS CAUSED BY ANORECTAL FISSURE

Report of Two Cases

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THE breast-fed infant receiving plenty of milk is seldom constipated, nor is the stool hard, well formed or copious. The fat, sugar, and protein of breast milk are so well absorbed that very little is wasted in the stool. The majority of cases of constipation in the breast-fed infant are of simple nature, but this fact does not preclude a careful examination of each patient with this complaint. This examination naturally includes inspection of the anorectal region and here often is found one of the common, less important, but very disturbing lower intestinal tract disorders of infants, namely anal or rectal fissure.

The stools of breast-fed infants are not large, hard or dry under normal conditions, and it seems highly improbable that such a small lesion could cause such a disturbance. The anal region is well supplied with nerves, however, and the slightest defecation at times causes extreme pain. Constipation is usually the result, and as this condition persists, the stools become larger, harder and drier; defecation becomes more painful, and a vicious cycle is present.

CASE REPORTS

Case 1.—G. B., aged four months, was brought in with a complaint of constipation of two and one-half months' duration. During the first six weeks of life, the bowel movements were perfectly normal, but since that time they have been irregular and accompanied by pain as evidenced by screaming and drawing up of the thighs in a flexed position. The stools were at times copious, hard, and dry and accompanied by the passage of much gas. No blood was observed in any of the stools.

History.—Full-term baby, normally delivered and breast fed; no history of any acute illness; has gained well since birth, and is on a four-hour-interval nursing schedule; has been getting cod liver oil and orange juice for the past two months.

Examination revealed a well-developed and nourished infant, weighing thirteen pounds and ten ounces. The head, neck, and thorax were negative. The abdomen was moderately distended with gas and a few small, hard masses were felt in the region of the sigmoid colon. These were thought to be masses of impacted feces. A small, red, slightly indurated area was found near the posterior portion of the anal opening, and at the base of this area a short linear tear was noted at the mucocutaneous junction. Rectal examination showed that the sphincter was rather spastic.

A bland ointment was used locally and mineral oil in small doses administered twice daily. The local redness and induration disappeared rapidly, the stools

gradually became more normal and there was no evidence of pain on defecation six days after the starting of treatment. Four weeks later the stools were perfectly normal and there was no recurrence of the constipation.

CASE 2.—M. S., aged seven months, was brought in with a complaint of constipation and colic of four months' duration. She had been well until three months of age when the bowel movements became irregular. On one occasion she did not have a movement for three days. Suppositories and enemas were resorted to, and this seemed to give relief for a few days. The mother stated that she had noticed a slight excoriation near the anus, and that at times the baby cried as if in pain when enemas or suppositories were used. No blood was ever noticed in the stools.

Past history.—Full-term, normally delivered, breast-fed infant, weighing 15 pounds and 14 ounces at six months of age. No history of any acute infections other than an occasional head cold; started on cod liver oil and orange juice at two months of age and cereals at six months of age.

Examination revealed a well-developed and nourished infant weighing 16 pounds and 5 ounces. A mucoid discharge from the nose was present and the throat was slightly red. The neck and chest were normal. The abdomen was not distended and no fecal masses were palpable. Examination of the anus showed nothing externally. Digital examination of the rectum revealed a very tight sphincter. A small nasal speculum was inserted into the rectum and a rather deep fissure on the posterior surface of the rectal mucosa was observed. This fissure was about one and one-half centimeters in length and had a rather broad, grey base. No blood was seen.

Lunar caustic was applied to the fissure on four occasions; mineral oil in small doses was given by mouth twice daily. Improvement was gradual in this case, and eight weeks after starting treatment the stools were normal. At the end of this period rectal examination with the speculum revealed a thin grey ridge at the site of the old fissure.

478 PEACHTREE STREET, N. E.

RENAL RICKETS

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THIS syndrome is sufficiently unusual to constitute a novelty when it is discovered. Most of the reports in the literature emanate from British sources. Kempson Maddox,[1] after an extensive and thorough investigation of the disorder reviewed the literature and added three new cases. Parsons[2] describes the roentgen appearance of the bones. The reports in this country to which reference should be made are those of Shipley[3] and his coworkers, Lathrop,[4] Swart,[5] and Schoenthal and Burpee,[6] who made extensive metabolic studies of a case.

Variously described by different authors as renal infantalism, renal dwarfism, or nanism, renal rickets and renal pseudorickets, it is characterized clinically by a stunting of growth, associated with skeletal deformities grossly resembling true rickets. There are knobbing of the ribs, Harrison's groove, pigeon breast, knock knees, anterior bowing of the shins, and enlargement of the epiphyses. If the patient survives until puberty, there is retardation of sexual development.

Underlying these manifestations, is a serious impairment of kidney function caused by a chronic nephritis. Although a similar symptom-complex is described as a result of long standing hydronephrosis, congenital polycystic kidney, or any similar or related condition which produces serious impairment of kidney function, this article will deal with the syndrome underlying, which there is, *sui generis*, a chronic nephritis.

Genu valgum (knock knees) is one of the most obvious symptoms and the one for which the patient usually seeks advice. The disorder is seldom discovered before the sixth or seventh year. The disease is insidious in onset and progressive in character. The renal manifestations are frequently masked by the skeletal abnormalities and are usually not discovered until the impairment in renal function has advanced to the stage of renal decompensation.

The renal part of the picture is in general that of a chronic glomerulonephritis. Polydypsia and polyuria are conspicuous symptoms. The skin is dry and coarse and often has a peculiar yellowish red tinge, not unlike bronzing. There is a tendency toward hemorrhage in the mucous membranes and skin. A secondary anemia is usually present. The blood pressure may or may not be elevated. Retinal changes related to the renal disturbance may or may not be present.

From the Pediatric Service of St. Vincent's Hospital, New York City.

The urine is pale, with fixation of the specific gravity usually below 1.010. It contains albumin in faint traces. Isolated hyaline casts and occasionally white and red cells in very small numbers are found.

In this stage of the disease where renal decompensation is present, the blood chemistry shows an elevation of the nonprotein nitrogen, urea, uric acid, and phosphorus. The calcium content of the blood is usually depressed, and there is a chronic acidosis.

The phosphate retention is apparently due to the inability of the kidneys to excrete this substance. The lowered calcium apparently occurs as a consequence of this.[7, 8, 9] A. Graeme Mitchell[10] offers the theory that some of the excess phosphorus is excreted into the intestinal tract, combines there with the calcium from ingested food, and forms insoluble calcium phosphate, which is not absorbed. There is, thus, failure of calcium absorption. A negative calcium balance and true calcium starvation occur. Further, as a result of impaired kidney function, there is an inadequate ammonia formation. In consequence of the failure of this important mechanism for the control of acid base equilibrium, the body is compelled to excrete fixed base in its attempt to combat and excrete the acid end products of metabolism. Among the fixed bases on which the body draws are those stored in the bones, and a general demineralization of the skeleton results.

Roentgenologically the evidence of this demineralization is seen in the extensive decalcification of the bones of the body. This is apparent from the rachitic changes in the epiphyses, rarefaction in the shafts of the long bones and similar pathologic changes in the skull, vertebrae, pelvis, and other flat bones.

The terminal picture is usually uremic in nature and occurs most frequently in the second decade of life.

Pathologically, except for the osseous changes described above, the most conspicuous alterations are found in the kidneys. They are small, sclerosed, and fibrotic. There is thinning of the cortex, destruction and disappearance of the glomeruli and tubules, and extensive interstitial changes. There is frequently found an hypertrophy of the heart and occasionally sclerotic changes in the blood vessels.

There is much speculation as to the etiology. Almost all writers who have studied the condition believe it to be a primary kidney complex resulting in disturbances of mineral metabolism. The impairment in kidney function causes this. There appears to be no common factor responsible for the kidney disease. Some investigators relate its origin to fetal life and intimate renal defect arising from germplasm. Toxemia of pregnancy has also been held responsible. Syphilis has been suggested as a cause for a few of the cases. Other infections and particularly those of a streptococcic nature, like scarlet fever, have been held responsible. The persistence of previous nutritional rickets has also been suggested. Exogenous poisons, such as lead and mercury, have

been suggested and finally the endocrine glands, the hypohysis, adrenal, and parathyroids have each been investigated as a possible etiological factor.

There is no consensus of opinion that any one factor will explain every case. The question of the etiology of renal rickets is obscure. The syndrome falls into the category of those diseases for which there is no definitely known cause.

Although the two cases reported here resemble those previously reported, they are, nevertheless, unique because of the fact that the patients are brothers. The familial incidence of this disease is, however, not new. A. Graeme Mitchell[10] infers family and hereditary predisposition to nephrosclerosis. Maddox[1] in his article notes a family history nine times in his review of the literature.

CASE REPORTS

CASE 1.—The elder of these two boys of Italian parentage was nine and one-half years old. He had been breast fed until the age of two years. He had never received cod liver oil or viosterol or any other antirachitic. Orange juice was not given until two years of age. Cereal and vegetable were started at eighteen months. He began walking and talking at two and one-half years, but never walked well. He had always had enuresis. He drank about one and one-half liters of water daily, in addition to other fluids. There was no history of previous illness. Weakness in the legs prompted the parents to seek professional advice about one month before admission to St. Vincent's Hospital. The family physician had previously referred them to an orthopedic hospital for an operation on the legs. At this hospital where the patient remained for nine days, it was decided the child was too weak for operation. (Many authors call attention to the danger of operating on knock knees because of the fact that there may be an underlying nephritis. They suggest that all such cases have a careful investigation, including a blood chemistry in order to exclude the possibility of nephritis before an operation is undertaken.)

Two days before admission to St. Vincent's Hospital, he began to bleed from the nose. Black and blue spots characterized by the mother as bruises had been noticed on the legs for about three months prior to admission. On the morning of admission to St. Vincent's Hospital, he refused his breakfast because he didn't feel well, complained of pain in the epigastrium, vomited dark red blood five or six times and bled from the nose. His breathing became heavy, and the child became stuporous, although he could be aroused.

The family history disclosed the fact that a brother had died one year previously at the age of seven years. He was characterized as an invalid who never developed properly.

Physical Examination.—Examination revealed a poorly developed and poorly nourished male child said to be nine and one-half years old although he did not appear to be more than five. He had the appearance of chronic illness. The skin of his face had a peculiar reddish yellow tinge. The skin was generally coarse and dry. The child was alert, looked apprehensive and worried, and asked for water constantly. His breathing was rapid and labored and gave one the impression of air-hunger. The superficial blood vessels of the body were full and dilated. Notably conspicuous in this respect were the vessels at the junction of the chest with the abdomen and the vessels of the upper eyelids. The child had a distinctly female habitus, flaring hips, and knock knees. There was an elevation of the tissues over the pubis resembling a mons veneris.

The blood pressure was 98 systolic. No abnormality about the skull was noted. The eyes, including eyegrounds, were negative. Ears were normal. The mucous membranes of the mouth were pale; those of the throat were slightly congested; and tonsils were bad. The teeth were hypoplastic and carious. There was no fullness about the neck, in the region of the thyroid gland, and no masses were felt in this region.

The chest was barrel shaped, emphysematous. The heart sounds were weak and lacking in muscular quality. No murmurs were heard. No enlargement was discerned clinically. The lungs were clear.

Fig. 1.—(Case 1.) Film of the upper end of both humeri shows a narrow zone of diminished density beneath the upper end of the shaft of the humerus on both sides. The trabeculations of the humerus are coarsened. The epiphyseal line is slightly cupped and irregular. The clavicles show rarefaction.

The abdomen was markedly distended, widened above and narrow below, tense and impossible to palpate satisfactorily. There was flaring of the lower rib margin.

Extremities: The legs were thin, spindly, atrophic, and showed a few ecchymotic spots. The joints were prominent and appeared enlarged.

Neurologic: The child was responsive, and there was no evidence of central nervous disease. Chvostek and Trousseau signs were absent.

The breathing became rapidly worse, deep, loud, and stertorous, not unlike that due to a diphtheritic laryngitis or obstruction due to a foreign body. Locally there

was no evidence to indicate diphtheria. The nose and throat cultures were negative for diphtheria bacilli. The throat culture grew hemolytic streptococci. Bronchoscopy revealed dryness and congestion of the pharynx, larynx, and tracheobronchial tree. No evidence of foreign body. X-ray photograph was also negative for foreign body and pneumonia. There was a slight enlargement of the heart to the left. The upper epiphyses of the humeri reveal rachitic changes. Rarefaction is apparent in the clavicle. (See Fig. 1.) The child died within forty-eight hours of admission.

Blood Count.—Hemoglobin, 68 per cent; R.B.C., 3,000,000; W.B.C., 19,950; polymorphonuclears, 86 per cent; lymphocytes, 13 per cent; eosinophiles, 1 per cent; bleeding time, 6½ minutes; coagulation time, 7 minutes; and platelets, 59,000.

Comment: No satisfactory explanation has been given for the tendency of these children to bleed. The blood counts reported heretofore have been normal except for secondary anemia. The diminution of platelets in this child is sufficient to explain the tendency to hemorrhage in this case.

Urine Report.—Three separate specimens were examined. The findings were the same in each: Albumin, trace. Sediment showed a few white blood cells. Specific gravity ranged from 1.009 to 1.010.

Blood Chemistry.—NPN, 125; plasma CO_2, 14 volume per cent; calcium, 5.6 per cent; phosphorus, 7.9 per cent; cholesterol, 165; chlorides, 550.

Comment: Note the high NPN, the profound acidosis, the depression of the calcium and the elevation of the phosphorus. In spite of the low calcium, tetany is apparently seldom found. The absence of symptoms of tetany in such cases is explained on the basis of a relative or absolute increase in the free or ionized calcium in the serum although the total calcium may be low.[11, 12] This increase in the ionized calcium is supposed to be a result of the acidosis,[13] the acidosis causing a mobilization of the calcium from the calcium reservoirs of the body.[14] In this instance, our figures refer to total calcium. The free or ionized calcium was not determined.

Postmortem Examination.—(Dr. Alexander Fraser.)

The brain revealed a moderate congestion and edema.

The thyroids and parathyroids were negative both grossly and by section.

The chest revealed numerous adhesions in the left pleural cavity. Both lungs showed congestion and edema in the lower lobes with emphysema in the upper lobes.

The heart showed slight hypertrophy of the left ventricle but otherwise the heart and blood vessels were normal. There was no evidence of atheromatous changes.

The stomach wall was swollen and the mucosa was hyperemic but no hemorrhages or erosions were present. The esophagus and intestines were normal.

The liver showed toxic necrosis.

The spleen showed chronic passive congestion.

The kidneys were small and very pale in color. The capsules stripped with difficulty and left a finely granular surface. On section, the cortex was very irregular in width and the cortical markings were completely obscured by whitish and grayish spots. The whole texture of the kidneys presented a mottled grayish and yellowish gray appearance.

The adrenals were normal.

The genital organs were negative.

Microscopic Report of the Kidneys.—

The glomeruli and tubules show widespread progressive atrophy with fibrous replacement. About 50 per cent of the glomeruli in a microscopic field are completely replaced by hyalinized fibrous tissue. From 80 per cent to 85 per cent of the glomeruli show some degree of atrophy and fibrous replacement. This fibrous replacement of the glomeruli appears to start in the capsule, which progressively

thickens as the glomerular tufts atrophy. The space left by the atrophy of the glomeruli is occupied by a cellular connective tissue. The distribution of this lesion is not uniformly diffuse. We see strands of relatively normal glomeruli, many of which are hypertrophied tubules, alternating with strands of scar tissue including numerous completely hyalinized glomeruli, atrophied tubules, and connective tissue. The glomeruli, being closely packed together, appear exceedingly numerous. The

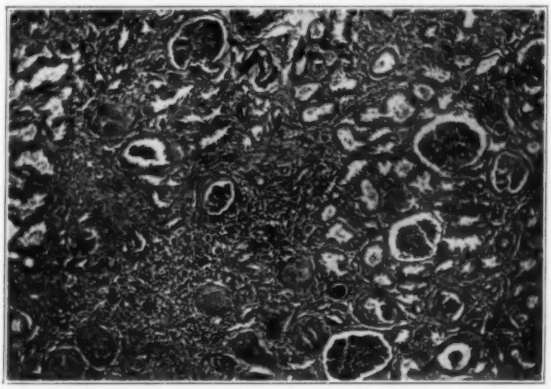

Fig. 2.—Renal scar tissue in center with hyalinized glomeruli, atrophied tubules and interstitial infiltration with lymphocytes and plasma cells. Functioning areas at right side, showing hypertrophied glomeruli and tubules at right hypertrophied tubules at left. (Case 1.)

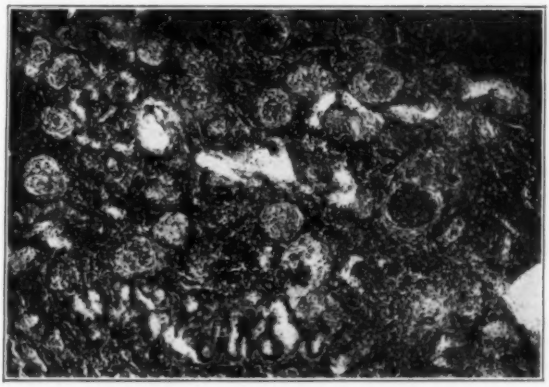

Fig. 3.—Numerous completely and several partially hyalinized glomeruli, with only one capable of function. Interstitial tissue densely infiltrated with lymphocytes and plasma cells. A few large tubules show granular degeneration, the remainder being either completely replaced by the cellular infiltration and fibroses or markedly atrophied. The latter appear as very small tubules lined by small epithelioid cells with densely straining nuclei. (Case 1.)

medium-sized renal vessels show the marks of hypertrophy. The preglomerular arterioles show a type of obliterating endarteritis which accompanies atrophy of the parenchyma rather than the hyaline deposits found in the intima in arteriosclerosis. The interstitial tissue is diffusely and rather densely infiltrated with lymphoid and plasma cells, presenting the histologic picture seen in so-called acute interstitial

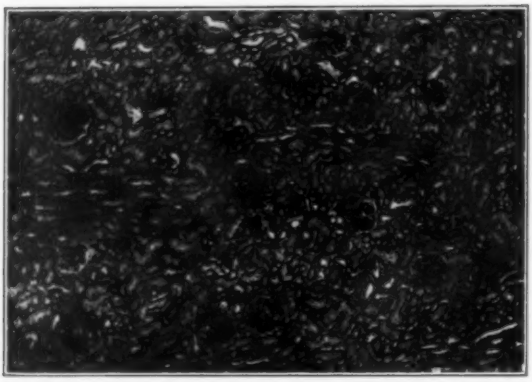

Fig. 4.—Normal kidney.

Fig. 5.—(Case 2.) There is an area of diminished density in the upper third of the right humerus which looks like a small bone cyst. Just beneath the epiphyseal line at the upper end of both humeri is a zone where the shaft is narrower and where the architecture is peculiar. The architecture of the lower third of the humerus is coarsened and shows decalcification.

nephritis commonly found in children. Although we are not familiar with a chronic form of this type of interstitial nephritis, it is quite possible that this case might be classed as such.

Figs. 2 and 3 are sections of the kidney of this case. Fig. 4 is a section of normal kidney for comparison.

Comment: The data in this case, clinical history and physical findings, x-ray pictures, urinalyses, and blood chemistry place this patient in the category of a renal rickets. The autopsy corroborates the diagnosis.

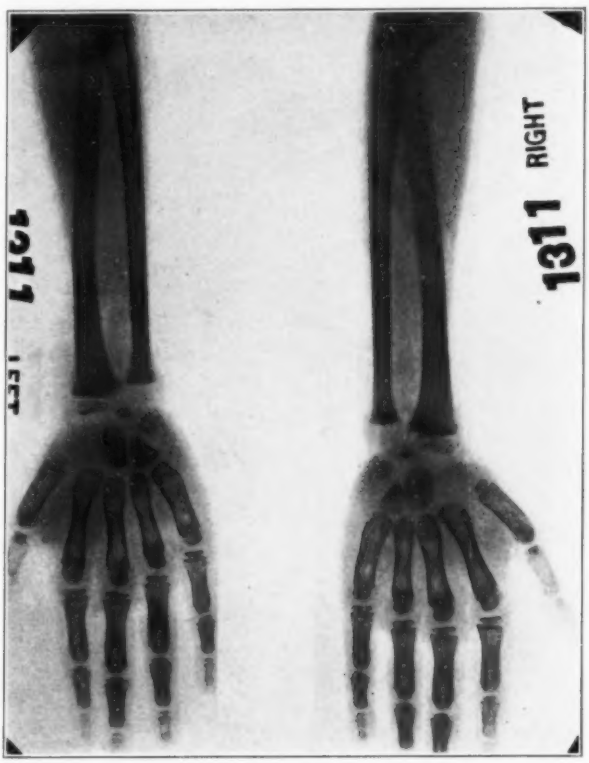

Fig. 6.—(Case 2.) The lower end of the ulna on both sides is cupped and shows a double line. The ulnar side of the lower end of the radius is slightly cupped and shows an abnormal calcium deposit in the cartilage appearing as lines of increased density radiating downward. The architecture of the bones of the forearm is slightly coarsened and there is evidence of decalcification. Both hands show a rather marked decalcification of the metacarpals and phalanges with thinning of the cortex and coarse irregular striations. The distal ends of the second, third, fourth, and fifth metacarpals appear cupped and a little shaggy.

Case 2.—The younger child, aged six years, was brought to the dispensary three weeks after the death of his older brother. The complaint was poor appetite and bedwetting. He had always had nocturnal enuresis. He was breast fed for ten months; orange juice was started at two months. He was given cereals and vegetables when he was twelve months old. At ten months of age, he was given Scott's emulsion, 1 teaspoonful three times daily for one year. Other than this no

antirachitic was given. He had a history of measles and bronchitis and pneumonia at five months of age. He also had otitis media, cervical adenitis, and occasional colds. For the past two years, the child had been failing. He had poor appetite, was weak and pale, drank a great deal of water, voided frequently, and wet the bed.

The physical examination revealed a pale, somewhat stunted child, who was fairly well nourished but poorly developed. He seemed to be active, happy, and bright.

The head, eyes, including eyegrounds, ears, and nose were negative. The mouth

Fig. 7.—(Case 2.) The bone of the neck of both femurs is more dense than the bone of the shaft, and is irregular in density. The epiphyseal line is irregular and there is decalcification just beneath its margin. There is evidence of decalcification in the shaft of the femur.

revealed pale mucous membranes, coated tongue, and carious teeth. The tonsils were negative.

The chest was symmetrical with a funnel-shaped depression over the sternum, Harrison's groove, flaring of the ribs, knobbing at the costochondral junctions. The lungs were clear, and the heart was negative. The abdomen was protuberant. An umbilical hernia was present. There were no palpable masses in the abdomen. Liver and spleen were negative.

There was an increase of the suprapubic fat.

Genitals were negative.

The musculature was weak and flabby.

The extremities were slender and atrophic. There was anterior bowing of the shins, slight knock knees and flatfeet. He stood with slight flexion at the knees.

Neurologic examination was negative.

Blood pressure was 102/54.

Measurements: Length, 40¼ inches (17 inches—vertex to umbilicus; 23¼ inches—umbilicus to feet); circumference of head, 20½ inches; circumference of chest, 20½ inches; circumference of abdomen, 17¼ inches; weight, 37 pounds. The

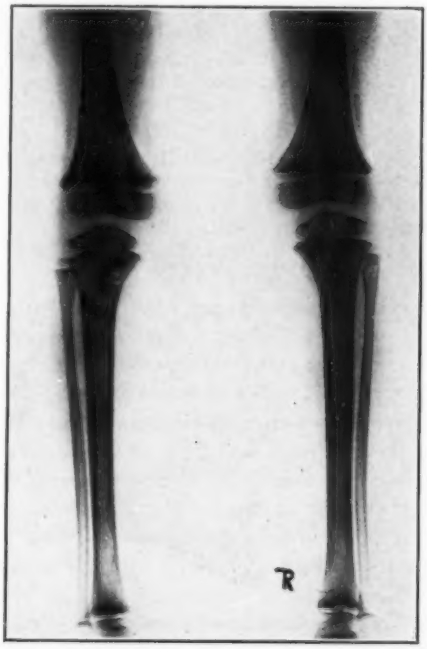

Fig. 8.—(Case 2.) The tibia and fibula show a slight generalized decalcification with coarsening of the trabeculae. The lower end of the shaft of the fibula on both sides is slightly but definitely cupped. The zones of preparatory calcification of the lower ends of the tibia and fibula are slightly widened and quite irregular along the epiphyseal margin producing a shaggy appearance. The appearance of the lower end of the femur is similar. The upper epiphysis of the tibia is shaggy but less marked than in the femur and the lower epiphysis of the tibia and fibula.

At the upper end of the right fibula is an oval area of diminished density which looks like a bone cyst. A smaller but similar spot is seen in the upper end of the left fibula.

child was somewhat short for his age, six years. (The dwarfism becomes more apparent with increasing age.)

Tuberculin reaction was positive; Schick, positive.

In view of the fact that this child resembled his brother in history and physical findings, a blood chemistry, complete x-ray of his skeleton, and urinalysis was ordered. This investigation was rendered somewhat difficult because it was necessary to secure the data in the dispensary, the parents having refused admission to the hospital.

Urine: Specific gravity, 1.003; albumin, trace; sugar, negative; sediment, showed an occasional white blood cell.

Blood chemistry (May) was as follows: NPN, 60.4; plasma phosphorus, 11.3; chlorides, 550; calcium, not done.

The blood count showed a mild secondary anemia and a 7 per cent eosinophilia, but was otherwise negative.

The x-ray findings were of interest and showed rachitic changes in the epiphyses and widespread evidence of decalcification throughout the skeleton. (Figs. 5, 6, 7, and 8.) The x-ray topography is consistent with a mild grade of renal rickets. In some places it appears that repair had taken place of a process which might have been worse some months ago. The story of this syndrome over a period of years may well be periods of exacerbation and remission, in which, during the periods of remission, there is better excretion of the phosphorus and better absorption of the calcium. The cystlike changes in the bones are of interest. We believe that parathyroid disease can be ruled out because of the low calcium, 8.7 mg. per 100 c.c.

The child was placed on 30 drops of viosterol once daily. He returned after five weeks.

The blood chemistry was repeated in July and is as follows: NPN, 54.1; urea, 32.4; uric acid, 6.1; creatinine, 2.0; chlorides, 570.0; sugar, 101.0; cholesterol, 250.0; plasma CO_2 C: P., 32 volume per cent; plasma albumin, 5.78; plasma globulin, 1.97; plasma phosphorus, 6.6; serum calcium, 8.7.

COMMENT

There is very slight reduction in the NPN from five weeks previously. The cholesterol is elevated slightly. Extreme degrees of lipemia are reported in this condition.[2] The child has acidosis; the phosphorus is elevated; the calcium is below the range of normal. During five weeks of viosterol therapy, the phosphorus decreased from 11.3 to 6.6. It is not known what the calcium was before antirachitic therapy. It was very likely low when compared with the phosphorus.[2, 13, 15] The chemistry suggests improvement following viosterol therapy, but there was x-ray evidence of repair before viosterol therapy was begun. One cannot say the improvement in chemistry in this instance was due to viosterol therapy. Most authors claim that antirachitics have no effect on this condition but György[16] claims a cure of this condition in one out of three cases following the use of vigantol (viosterol). Karelitz'[17] case is suggestive, but not conclusive. On purely theoretical grounds, one should not expect improvement from this form of therapy.

Lack of cooperation on the part of the parents interrupted further investigations on this child. We believe that clinical history, the x-ray findings, blood chemistry, and urinalyses furnish us with sufficient data to place this patient in the category of a renal rickets. The pathology in the underlying kidney condition is a matter of conjecture. By analysis, however, we venture the belief that the kidney pathology is not dissimilar from that of the older brother.

RÉSUMÉ

The syndrome called renal rickets is described. We report two instances in brothers, nine and one-half and six years old, respectively.

The former is accompanied by an autopsy protocol. We emphasize the importance of a careful investigation of all children with knock knees.

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REPORT OF THREE CASES OF CONGENITAL HEART-BLOCK WITH A RÉSUMÉ OF THE LITERATURE TO DATE

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IN 1929 Yater[1] reviewed the literature on congenital heart-block and collected thirty cases. He discarded many cases in which he regarded the diagnosis as unjustified and suggested that this diagnosis should be made only in cases in which heart-block was demonstrated by electrocardiographic examination; in which a slow pulse had been noted at an early age; and, in which there was no history of rheumatic fever, chorea, diphtheria or congenital syphilis. At about the same time Davis and Stecker,[2] reviewed the literature and added one more case of complete heart-block. The case of partial heart-block reported in 1929 by Nicolson, Shulman and Green[3] was not included in Yater's series. Brandenberg,[4] Anderson,[5] Leech,[6] Selar,[7] and Koenen[8] have each reported a case of congenital complete heart-block. Maude Abbott[9] in a recently revised article on congenital heart disease mentions a case of partial block reported by Baumgartner and Abbott,[10] and in the same article, a case of complete block from Moffatt's service, as yet unpublished, is described. These make thirty-nine cases recorded which, with the three reported here, bring the total to forty-two.

Postmortem studies have been published in only four cases. Wilson and Grant[11] reported the pathologic findings in a fourteen-month-old infant with partial heart-block, cyanosis, and clubbing. The autopsy showed complete atresia of the root of the pulmonary artery with a large patent ductus arteriosus in a triloculate heart. On the posterior wall of the common ventricle was a rounded muscular prominence, a rudiment of the interventricular septum. Histologic studies showed the auriculoventricular bands "reduced to a number of fine strands which pursue their course encased in dense fibrous tissue."

In Yater's case[1] there was reported incomplete heterotaxy with complete separation of the auriculoventricular node from the bundle of His. Perotti's case showed complete absence of the membranous portion of the interventricular septum; the right auricle communicated with the left ventricle. In this instance no histologic data are given. Maude Abbott mentions a case of congenital complete heart-block from Moffatt's service in which the heart "presented a remarkable combination of displaced left auricle, transposition of the great arterial trunks, double mitral ostium, cor biatriatum triloculare, with right conus stenosis and congenital pul-

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TABLE 1*

CASE	AUTHOR	SEX	AGE WHEN PROVED	AGE WHEN SLOW PULSE FIRST NOTED	PROBABLE MALFORMATION	CARDIAC ENLARGEMENT	GRADE OF BLOCK	SLOWEST VENTRICULAR RATE	CYANOSIS	OTHER OBSERVATIONS
31	1928 Davis and Stecker	M	13 mo.	13 mo.	Interventricular septum defect	Moderate	Complete	47	None	No symptoms
32	1928 Brandenberg									
33	1929 Nicolson, Shulman, and Green	M	12 mo.	12 mo.		Moderate	Partial, varying 3:1, 2:1, 4:1	78	Slight, at times none	At 5 mo. attack of coughing with cyanosis and syncope
34	1929 Anderson	M	7 yr.	7 yr.	Patent interventricular septum	Marked	Complete	48	None	At 7 yr. one attack of syncope
35	1929 Baumgartner and Abbott									
36	1930 Leech	F	8½ yr.	4½ yr.	Patent ductus arteriosus ? patent interventricular septum	Moderate	Complete	48	None	
			14 yr.							
37	Sclar.	M	8 mo.	4 yr.		Moderate	Complete	48	None	Right ventricular preponderance
38	Koenen	M	9 mo.	9 mo.		Slight	Complete	52	None	
39	Moffatt's (from Nelson)		20 yr.		Multiple		Complete		Present	
40	Author's case	F	9 yr.	9 yr.	Interventricular septal defect	Marked	Complete	48	Very slight	
41	Author's case	M	5 yr.	4 yr.	Interventricular septal defect	Marked	Complete	44	None	
42	Author's case	F	3 yr.	3 yr.	Interventricular septal defect	Moderate	Complete		None	Frequent Adams-Stokes attacks and death during one

*The first thirty cases are recorded by W. M. Yater, Am. J. Dis. Child. 38: 112, 1929. These are the cases reported since that time.

monary arteriovenous aneurysm.'' It will be noted then, that the four autopsy reports in the literature show this condition to be dependent upon a developmental defect of the auriculoventricular bundle rather than upon a fetal endomyocarditis.

This report is concerned with a brief description of three cases of complete heart-block believed to be congenital. One of the children (in Case 3) had frequent Adams-Stokes attacks and presumably died in an attack of syncope. The other two (in Cases 1 and 2) appear to be normal and have no symptoms of heart disease.

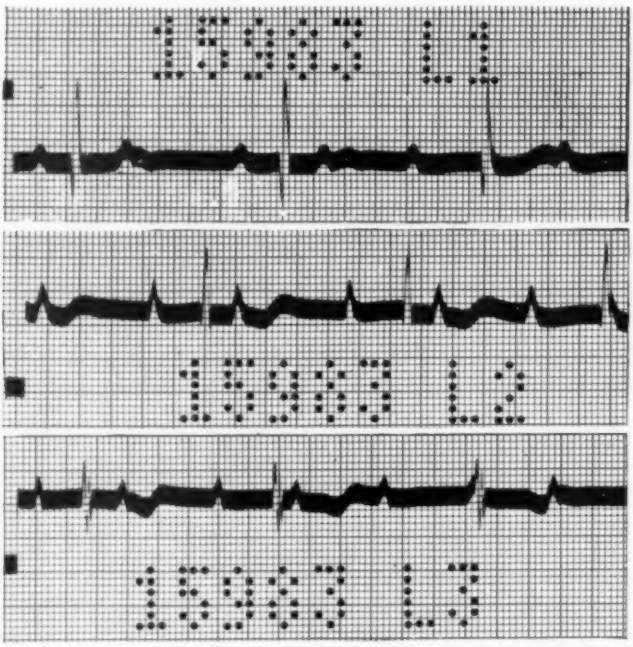

Fig. 1.—Complete heart-block, ventricular complexes of the supraventricular type, splintering of QRS in Lead III, and an auricular arrhythmia.

CASE 1.—This patient, a girl, nine years old, was brought to the hospital in October, 1931, for examination as to the possibility of a tuberculous infection because her father died of this disease six years before. Her parents had been told that her heart was very slow during an attack of pneumonia when she was six months old, but she had never been cyanotic nor experienced dyspnea or edema. She had been normally active for her age.

The patient was fairly well nourished and well developed. The heart was definitely enlarged; a heaving apex beat was felt in the fifth left interspace, 2 cm. outside the nipple line and 10 cm. from the midsternal line. There was a distinct diastolic thrill over the fourth left costal cartilage. On auscultation a very loud, harsh, prolonged diastolic murmur was heard best at the fourth left costal cartilage. Higher up, at the second costal cartilage, this murmur became blowing, and it could also

be heard nearly to the apex but lost its harsh character there. Along the left border of the sternum, there was a harsh systolic murmur, loudest in the second interspace. The heart rate was 48 per minute. The systolic blood pressure was 110 mm. of mercury, the diastolic 65. A definite capillary pulse was seen. The remainder of the physical examination showed nothing definitely abnormal.

The clinical diagnosis was complete heart-block, congenital heart disease, with a probable defect in the ventricular septum.

Laboratory Findings.—The routine examination of the blood showed nothing abnormal. The Kahn test was negative. A roentgen examination of the chest showed gross cardiac enlargement with reduction of the upper portion of the retrocardiac

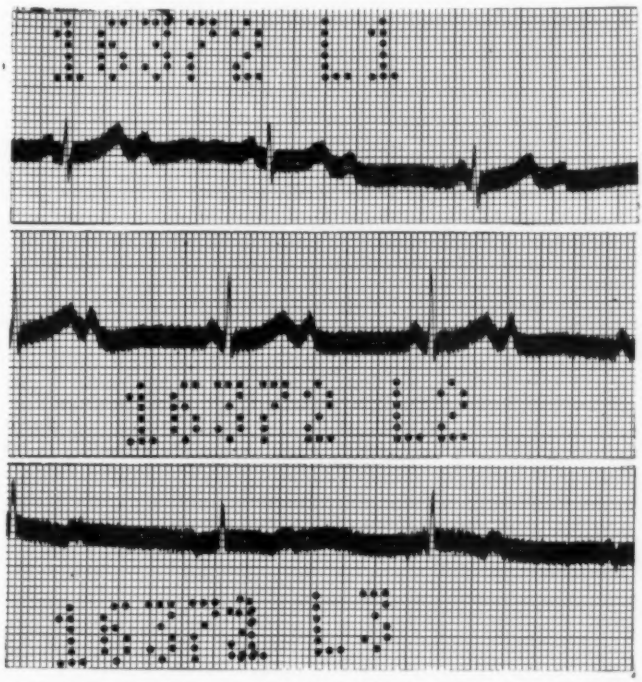

Fig. 2.—Complete heart-block, ventricular complexes of the supraventricular type, and an auricular arrhythmia.

space corresponding to the location of the auricles, and an increase in the transverse diameter of the heart shadow suggesting a slight preponderance of the left side.

The electrocardiogram taken October 19, 1931, is reproduced in Fig. 1. It shows complete heart-block with an auricular rate of 112 per minute and a ventricular rate of 47 per minute. The ventricular complexes are of the supraventricular type, and are normal except for an unusual amount of splintering of QRS in Lead III. There was a distinct auricular arrhythmia; the auricular cycles which contain a ventricular beat tend to be shorter than the others. The auricular complexes are normal in outline.

Reexamination on April 27, 1932, showed a heart rate of 48 while quiet, 52

after exercise. On auscultation a diastolic and a systolic murmur were heard best along the left border of the sternum. The electrocardiogram was identical with that previously taken.

CASE 2.—The patient, a five-year-old boy, came to the hospital on January 14, 1932. There was a history of pertussis, varicella, pneumonia, and frequent attacks of tonsillitis. His heart had been examined during the attack of pneumonia two years before by his home physician, who had mentioned no abnormalities. In May, 1931, however, an examination was made by a school physician who told his parents that he had a slow pulse and an abnormal heart. He had been kept in bed or on

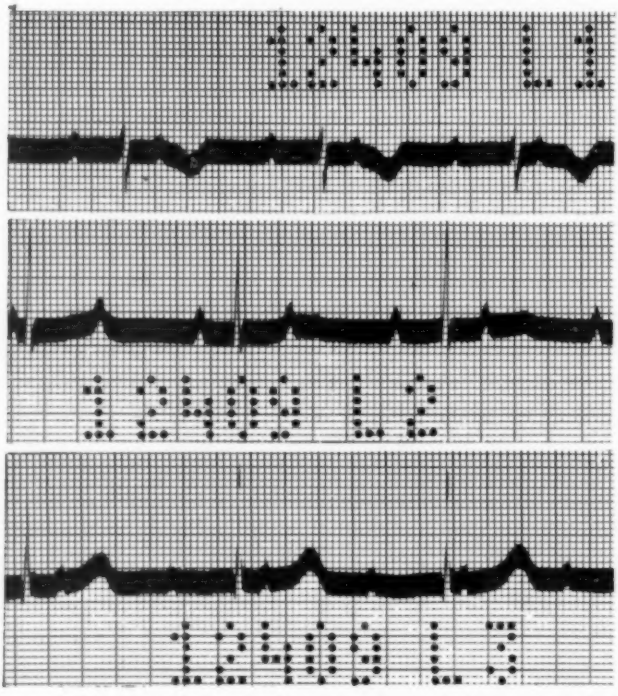

Fig. 3.—Complete heart-block, ventricular complexes of the supraventricular type with moderate right axis deviation, inversion of T-wave in Lead I, and an auricular arrhythmia.

limited activity since that time. A poor appetite was the chief symptom noted by the parents. Neither cyanosis nor dyspnea had been observed.

The patient was well nourished and well developed. The heart was definitely enlarged. The left border of cardiac dullness was 8 cm. from the midsternal line in the fifth intercostal space and the right border, 2 cm. The heart rate was 44 per minute; the rhythm regular. On auscultation a systolic murmur was heard in the midprecordium, loudest near the apex and along the left border of the sternum, and faintly heard in the back. It was transmitted to the carotids. There was a short, rough, early diastolic murmur at the apex. There was no cyanosis, clubbing, edema, or dyspnea. The systolic blood pressure was 108 mm. of mercury, the di-

astolic was 54 mm. of mercury. The remainder of the physical examination and routine laboratory tests showed nothing abnormal. The Kahn test was negative.

The clinical diagnosis was complete heart-block, probable congenital heart disease with interventricular septal defect.

The electrocardiogram taken January 13, 1932, is reproduced in Fig. 2. It shows complete heart-block with an auricular rate of 95 per minute and a ventricular rate of 47 per minute. The ventricular complexes are of the supraventricular type and are normal in outline. There is an auricular arrhythmia similar to that seen in Fig. 1.

The patient returned to the clinic every two months. He has gained in weight and his general condition is very good. The heart and electrocardiogram remained the same. He was allowed normal activity.

CASE 3.—The patient, a girl, aged three years, was brought to the University Hospital on September 27, 1929. Nothing abnormal was noted by the family physician at the time of her birth, but her heart rate was said to have been slow always. In 1928 she fell and was unconscious for two hours. She had never been cyanotic and had had no acute infections. About three weeks before coming to the hospital she had several attacks of pain with convulsions after eating pop corn. A physician who saw her in one of the attacks stated that she became stiff, her eyes rolled up, and her face became pinched and drawn. There were no convulsive movements. Her pulse is said to have disappeared completely. Artificial respiration was administered. The attack did not last more than two or three minutes; her face was deeply cyanosed during the last part of the attack. The pulse was usually about 65 per minute. Belladonna had been given but had not increased the pulse rate.

On examination the heart was definitely enlarged. A loud systolic murmur and a short, rough diastolic murmur were heard at the apex. The systolic murmur was equally loud at the base. The auricular sounds could not be clearly heard. There was no cyanosis. The rest of the physical examination was entirely negative.

The clinical diagnosis was complete heart-block with Adams-Stokes attacks, congenital heart disease, and ventricular septal defect.

The electrocardiogram showed complete heart-block with an auricular rate of 112 per minute and a ventricular rate of 50 per minute. The ventricular complexes are of the supraventricular type. They show moderate right axis deviation, and there is marked inversion of the T-deflections in Lead I. A distinct auricular arrhythmia of the type previously mentioned was present.

According to the patient's physician, Dr. E. R. Robbins of Detroit, who has been good enough to supply us with information regarding the outcome, she continued to have Adams-Stokes attacks, and was usually revived by vigorous stimulation of the anal sphincter. Death occurred in January, 1931, presumably in one of these attacks, but no physician was present. No autopsy was obtained.

COMMENT

Table I is a compilation of the cases recorded since Yater's report and is a tabulation similar to the one of White, Eustis and Kerr.[12] This table also includes the writer's three cases.

It is my impression that all of these cases should be considered examples of congenital heart-block. All of the patients appeared to have congenital heart disease, and the most probable defect in each instance was an imperfect ventricular septum. This diagnosis was based on the presence of enlargement of the heart with a loud systolic and a

short, rough diastolic murmur, best heard in the midprecordium, but without cyanosis. It would seem probable that this lesion is likely to be associated with imperfect development of the atrioventricular conduction system. We regard the association of complete heart-block with the lesion as strongly suggesting that the conduction defect is congenital rather than acquired. In all three cases a slow pulse was noted at an early age and in all there had been no other condition to which heart-block might be attributed with the exception of frequent attacks of tonsillitis in Case 2.

Adams-Stokes attacks are apparently not particularly uncommon. There were nine cases showing these attacks among the thirty-nine cases of congenital heart-block that have been recorded. Many of these patients experienced no symptoms of heart disease.

In all of our cases the ventricular complexes of the electrocardiogram were of the supraventricular type indicating that the conduction defect lay above the bifurcation of the His bundle and that the two main branches of the His bundle functioned in a normal way. The ventricular rate was higher than is usual in complete heart-block in adults, and auricular arrhythmia was conspicuous.

In the absence of Adams-Stokes attacks congenital heart-block probably produces no symptoms and does not tend to shorten life. The prognosis depends upon the associated lesion.

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LYMPHANGIECTASIS WITH CHYLORRHEA

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THE consideration of conditions which may result from obstruction and dilatation of the peripheral lymph vessels, apart from elephantiasis, leads naturally to recording unusual and rare conditions of less clinical importance. Few cases of lymphangiectasis with chylorrhea have been reported during the past two decades. In spite of the apparent rarity of the clinical condition, it is difficult to believe that cases similar to one about to be reported have not been observed in this country.

CASE REPORT

J. S., a colored boy, eleven years old, was seen on July 9, 1931, with the complaint of swelling of the upper part of the left thigh and an intermittent milky white discharge from some small vesicles in the left groin. The mother stated that the child was in good health until about one year before entrance when he told her his left leg was wet. Upon examining the patient, she found a milklike fluid coming from a small vesicle on the left groin. The left thigh seemed larger, but the patient experienced no pain. The swelling of the thigh and drainage have occurred spontaneously and periodically since that time. The intervals were irregular varying from days to months. For the past few months the thigh has remained swollen and drainage has occurred with greater regularity. The vesicles in the left groin would rupture and discharge a characteristic milky fluid upon the slightest trauma. The mother volunteered the observation that the swelling in the thigh is less marked in the morning before arising, and the drainage of the milky fluid is increased by the ingestion of candy and decreased after castor oil catharsis. No pain or discomfort has been noted at any time.

Past History.—Measles at four years; mumps at six years; repeated attacks of tonsillitis for the past few years. History is otherwise uneventful.

Family History.—Father's whereabouts unknown. Mother has had two miscarriages after patient was born. No history of tuberculosis was obtained.

Physical Examination.—The patient is a fairly well-nourished boy. Positive physicial findings consisted of a moderate generalized lymph adenopathy and an obvious disproportion in size of the lower extremities. The upper third of the left thigh was distinctly larger than the right. The left inguinal region was fuller than the right and several discrete, millet-seed sized vesicles, filled with a whitish fluid, were noted in the skin. On the inner aspect of the left thigh, the perineum, and

	RIGHT LEG		LEFT LEG	
	7:30 A.M.	7:30 P.M.	7:30 A.M.	7:30 P.M.
Mid-thigh	35.5 cm.	36.1 cm.	37.1 cm.	38.0 cm.
Mid-calf	23.6 cm.	23.9 cm.	25.2 cm.	26.3 cm.
Ankle	16.6 cm.	17.8 cm.	19.8 cm.	20.6 cm.

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the left side of the scrotum up to the raphe the vesicles were more numerous and smaller. While the left leg was larger than the right, no definite change was noted in the daily measurements upon arising and retiring.

One of the larger vesicles in the groin was punctured, and a milklike fluid continued to drain. The rate of flow was not grossly altered by standing, lying down or by elevating the leg. Several ounces of fluid could be collected before the drainage

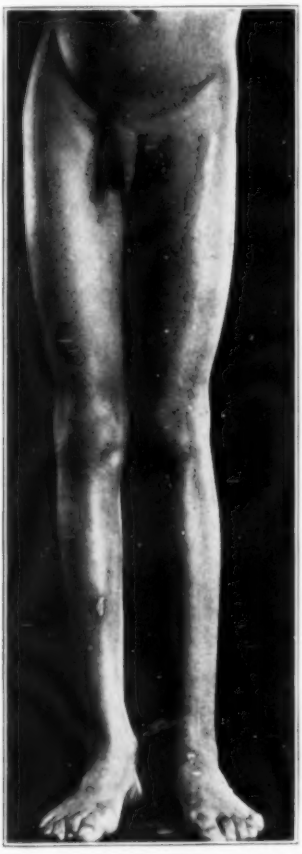

Fig. 1.—Photograph showing drainage of chyle from dilated lymph space located on the lateral aspect of the left leg. On the medial aspect is a group of dilated lymph spaces filled with chyle.

ceased spontaneously. The fluid was thin, milk white, and opaque. It clotted in from 5 to 10 minutes, when collected in a test tube. The clot was soft and nonretractile. Microscopic examination of the fluid revealed lymphocytes, a few red cells, and free fat globules. Culture of the fluid gave no growth.

Because the fluid in the vesicles was suspected of being chyle, an attempt was made to study the composition and drainage after a high fat meal. The following results were obtained after a meal at 12 noon:

		CHOLESTEROL	FATTY ACID	LECITHIN
1st specimen	1:30 P.M.	53 mg.	149 mg.	7.5 mg.
2nd specimen	3:30 P.M.	57 mg.	179 mg.	10.8 mg.
3rd specimen	5:30 P.M.	56 mg.	159 mg.	8.7 mg.

Laboratory Data—

Urine: Negative.

Blood: Hemoglobin 70% (Sahli)
Red Blood Count 4,850,000
White Blood Count 6,800
Differential
48% polymorphonuclears
33% lymphocytes
17% monocytes
2% basophiles

Serology: Blood, Wassermann and Kahn, 4 plus.
Spinal fluid, Wassermann and Kahn, negative.
Fluid from the vesicle, 4 plus.

COMPARATIVE CHEMISTRY OF THE BLOOD AND FLUID FROM THE VESICLE

BLOOD		FLUID FROM THE VESICLE	
Sugar	98.0 mg.	Sugar	114.0 mg.
NPN	31.0 mg.	NPN	26.6 mg.
Chlorides	505.0 mg.	Chlorides	586.0 mg.
Calcium	9.0 mg.	Calcium	8.8 mg.
Phosphorus	5.50 mg.	Phosphorus	3.24 mg.
Potassium	19.8 mg.	Potassium	18.6 mg.
Cholesterol	263.0 mg.	Cholesterol	53.0 mg.
Serum albumin	4.2%	Total protein	3.87%
Serum globulin	1.8%	Albumin	2.88%
CO_2	64.0	CO_2	58.0
P_H	7.47	P_H	7.28

Tuberculin: Mantoux Test, negative.

X-ray examination of the gastrointestinal tract and abdomen: Negative.

The clinical course of the patient was uneventful. No fever was present at any time during the observation, and the patient was in an apparently good state of health. Biopsy of one of the vesicles was undertaken. A milky fluid draining profusely from the biopsy wound was eventually controlled by pressure. Histologically, the vesicle was a dilated lymph space without any pathologic infiltration or proliferation of tissue. Although the patient presented no other clinical evidence of syphilitic infection other than generalized lymph adenopathy and positive serology, antisyphilitic treatment was instituted. After three complete courses, the serology remained unchanged. No changes in the left groin were observed.

The patient was under observation for two years and then moved to a different city. Returning to Chicago on July 27, 1933, he was readmitted to the hospital. During his absence the chyle ceased draining from the groin; however, the entire left leg increased in size, and chyle drained from the ventral surface of the toes. The vesicles on the scrotum increased in number but were not distended with chyle as they had been on his previous entrance. Because of the progressive character of the patient's illness, an exploratory laparotomy was decided upon. Upon opening the abdomen the mesentery was found to be studded with enlarged lymph glands especially marked about the small intestine. No other pathology was noted. A few glands were removed for histologic study and on section showed changes characteristic of a chronic lymphadenitis.

DISCUSSION

The causes of lymphangiectasis with chylorrhea are not definitely known. Numerous theories are offered to explain the condition. The most prominent hypotheses are those of Haferkorn,[1] Neumann,[2] and Ning.[3] The first author advanced the idea of a congenital defect in the anlage of the lymph spaces with subsequent dilatation due to stasis and congestion. Neumann,[2] however, believed that clinically and histologically this theory could not be substantiated. The author held to the idea of an abnormal communication with the lymph vessels of the thigh and chylous vessels on the same side. As most cases occur at about the time of puberty, the increase in blood pressure, incident to that period of age, raises the lymph pressure. The combination of increased pressure and a congenitally weak lymph vessel causes it to dilate. The explanation of the predilection for the occurrence on the inner side of the thigh and genitals is that the lymph spaces in this region are thinner, more superficial and more abundant. Hence, dilatation would be more likely to occur in these areas. Ning,[3] in a recent article, supports the idea of back pressure and congenital communication with the chyle vessels and lymph vessels of the thigh. He reports a patient who was very carefully studied and observed for a period of twenty-three years and in whom no change in the clinical condition was noted, except for an increase in the number of lymph cysts. It would seem to be more than a passing coincidence that in most of the cases reported, either syphilis or tuberculosis has been present. However, it is difficult to believe that this alone is sufficient to explain the condition. The number of cases of lymphangiectasis with chylorrhea are too few in number to be ascribed to such a common etiology alone. No postmortem studies are available, and rarely has it been possible to test the various theories clinically. Until conclusive evidence is presented, it would seem more feasible to leave the question of the pathogenesis open.

The mechanism of the appearance of chyle in the dilated lymph spaces is interesting. Despite the definite clinical findings in the cases reported, no satisfactory explanation has been offered of the lymph stasis. The predilection for the development of lymphangiectasis on the inner surface of the thigh and genitals is well supported anatomically, as Neumann pointed out. The lymph spaces in these regions are very abundant, have thin walls, and are superficial. Any increase in pressure would be more likely to be followed by external dilatation here than any part of the body. The presence of chyle in the dilated lymph spaces, however, presumes a retrograde stasis. Under such a condition only two explanations seem feasible—either a congenital, abnormal communication between a chyle vessel and one of the lymphatic vessels of the lower extremity or obstruction of the chyle flow into the thoracic duct by a luetic

or tuberculous gland. The latter possibility is illustrated by the diagram in Fig. 2. An area of obstruction is considered in the region of the celiac nodes. The diagram illustrates the normal course of lymph flow along the right iliac artery and the partial reversal along the left, resulting from an area of obstruction in the celiac nodes. Because of this obstruction, chyle coming from the intestine is prevented from passing into the thoracic duct via its main intestinal trunk, and is forced to find ac-

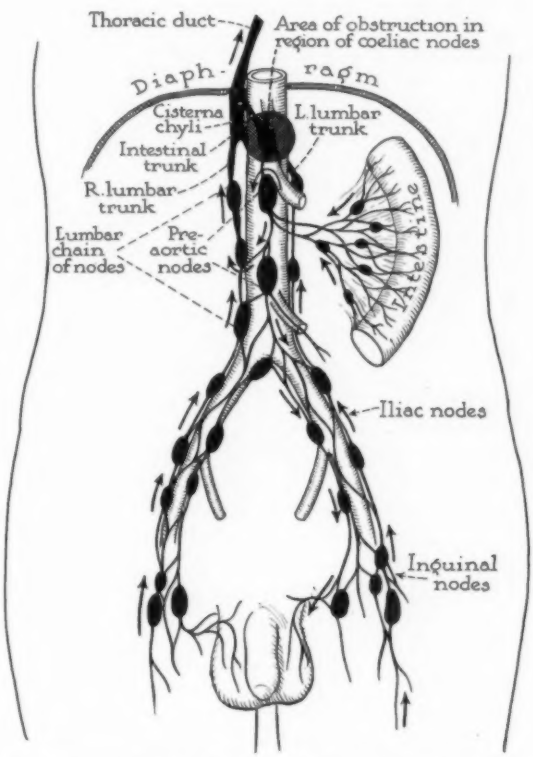

Fig. 2.—Diagram showing possible mechanism of lymphangiectasis with chylorrhea in this case.

cessory anastomoses to reach that duct. During the period of increased flow following digestion, these anastomoses are inadequate to carry the load. Much of the chyle backs up into the ileac lymphatics even to the extent of distending their superficial tributaries—the skin region of the femoral trigon and scrotum. The profusion of broad spaced lymphatic plexus with thin walls in these areas, in which the skin, as well as the superficial fascial layer, is thin, permits such vessels to become easily distended by back pressure.

SUMMARY

A case of lymphangiectasis with chylorrhea is reported. The question of pathogenesis is discussed, and evidence is presented to explain its occurrence as a result of acquired disease.

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THE DIAGNOSTIC TUBERCULIN REACTION

An Evaluation of Total Protein Tuberculin (Seibert) and Dermotubin (Löwenstein)

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THE diagnostic importance of the tuberculin test is well recognized at the present time. There is much less general agreement, however, regarding the type of reaction which is best suited to general practice. Since Koch's original experiment, a large number of technics have been devised for applying the test. Many of these have been abandoned. The principal procedures in vogue at the present time are the cutaneous test usually employed by the scarification method of von Pirquet, the intradermal reaction of Mantoux, and the subcutaneous test or one of its modifications. Other tests, such as the percutaneous reaction of Moro and the conjunctival reaction of Calmette and Wolff-Eisner, are used to some extent in various sections of the world but are not at all extensively employed in America.

The purpose of this investigation was to evaluate several commonly employed methods of tuberculin testing with relation to each other. In this regard we were especially interested in two procedures which are comparatively new: first, the use of a purified protein tuberculin (TPT. Seibert); and second, the evaluation of a percutaneous reaction using a tuberculin ointment devised by Löwenstein designated as dermotubin. To test these materials, simultaneous tuberculin reactions were given on all patients admitted to the Cook County Children's Hospital in the following manner: On the right forearm an intradermal reaction was given with 0.1 c.c. of a 1:100,000 solution of TPT. (Seibert) yielding 0.001 mg. of purified tuberculin protein to the dose. On the upper portion of the left forearm in a corresponding area an intradermal injection of 0.1 c.c. of a 1:1,000 solution of Koch's old tuberculin (Meister, Lucius, and Brüning, Hoechst, A. M.) in normal salt solution, giving a dose of 0.1 mg. OT. On the lower portion of the left forearm a Pirquet test was given using the same OT. undiluted, and on the thorax over the upper end of the sternum a dermotubin test was given using Löwenstein's ointment. In this manner interesting data were obtained relative to the incidence of the positive tuberculin reaction in this group of the population, and also the comparative value of the different methods could be assayed.

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The TPT. (Seibert) used in this investigation was supplied by Parke, Davis and Co., Detroit, Michigan.

This report comprises the results of such routine testing in 647 consecutive admissions to the wards of the Cook County Children's Hospital. All types of cases were included, admissions to the general medical wards, the surgical ward, the orthopedic ward, and the children's venereal ward. The medical cases included a small group of children with clinical tuberculosis. The distribution according to age is given in Table I.

TABLE I

DISTRIBUTION OF TUBERCULIN REACTION ACCORDING TO AGE

	NEGATIVE TO ALL TESTS		POSITIVE TO 1 OR MORE		
AGE	NUMBER	PER CENT	NUMBER	PER CENT	TOTAL
6 mo. to 2 yr.	87	82.9	18	17.1	105
2 yr. to 5 yr.	125	78.2	35	21.8	160
5 yr. to 10 yr.	170	74.3	59	25.7	229
10 yr. to 15 yr.	80	52.3	73	47.7	153
Total	462	71.4	185	28.6	647

Comparatively few infants were included; most of the patients ranged in age from two to fifteen years. Most of the children were white although there was a fairly large representation of colored races (30 per cent), principally negroes. From the sociologic standpoint, these cases were drawn from the lowest strata of urban population. Most of them came from overcrowded sections of the city where opportunity for contact with open tuberculosis should be great. The geographic distribution reveals that most of these children were living in the congested districts of the west side in the immediate vicinity of the hospital and in the colored sections of the south side. An attempt was made to correlate the reactions with a definite contact history, but in common with previous experiences with similar groups of people, it was found that reliable histories were unobtainable in most cases.

METHOD

All four reactions were carried out simultaneously upon admission except in a few cases of known active tuberculosis or where obvious tuberculin hypersensitivity was present, e.g., phlyctenar disease of the eye. The intradermal and Pirquet reactions were carried out in the usual manner. The dermotubin test is less familiar in America. This is a modification of the Moro reaction and is carried out in a manner similar to that of all percutaneous tests. According to Löwenstein,[1] the ointment consists simply of a concentrated glycerin bouillon culture of tubercle bacilli in which no other ointment base is used except the glycerin contained in the media. It consists, therefore, of concentrated tuberculin and killed bacilli. The material is supplied in small, glass-stoppered vials or 1 c.c. collapsible tubes. The skin over the upper end of the sternum is thoroughly cleansed with ether or benzene to remove the fat, a small drop of ointment is placed on the prepared skin and gently rubbed with the finger or with a small glass rod for about a minute. The skin is then left exposed to the air for ten minutes. The reaction is best read at the end of forty-eight hours though occasionally it reaches its height in seventy-two hours. A positive reaction consists in the appearance of typical pale red, pinhead-

sized papules, from one to thirty or forty in number, usually located on an erythematous base. One typical papule suffices for a diagnosis. Three degrees of positive reactions are described: (1) papules, (2) confluence of these papules into a patch of erythema from 3 to 5 cm. in diameter, and (3) vesiculation. Some experience is necessary in recognizing typical papules, but the reaction is very characteristic. Its great advantage lies in the ease and painlessness of application.

Total protein tuberculin (TPT. Seibert) consists in a highly purified principle isolated from tuberculin as a result of the comprehensive series of experiments conducted by Seibert[2] and her associates. This material is practically pure protein and yields clear-cut reactions in high dilution in tubercle-infected individuals. The material was supplied for this experiment by the manufacturer in vials containing a compressed tablet of 0.01 mg. tuberculoprotein. A properly buffered diluent was supplied in a separate vial. When ready for testing, 1 c.c. of the diluent was introduced into the vial containing the tablet of TPT., which was then dissolved. One-tenth c.c. of the resulting solution was injected intradermally into the right forearm,

Fig. 1.—Typical positive dermotubin reaction. (72 hours.)

yielding a dosage of 0.001 mg. of tuberculin. The material was thus always used freshly diluted. Reactions were read at the end of forty-eight hours.

The criteria adopted for the diagnosis of a positive tuberculin reaction, other than the dermotubin, were: (1) the presence of definite induration, and (2) a minimum diameter of 1 cm. Erythema without induration was considered a negative reaction. Only the strengths of tuberculin mentioned were used; since after preliminary testing, they were considered to be most desirable for routine use although it was recognized that a small proportion of infected individuals with low degrees of sensitivity would be missed. Since D'Arcy Hart[3] states that 0.1 mg. OT. intradermally carries a diagnostic error of from only 4 to 6 per cent for all age groups, it was felt that such a test would constitute an effective check in comparison with the new materials studied.

RESULTS

In a series of 647 consecutive children a positive reaction to one or more of the tests was obtained in 185, or 28.6 per cent (Chart 1). Of this number, 111 reacted positively to all tests. In the case of indi-

vidual tests the highest percentage of positives was obtained with the intradermal reactions. Here the total protein tuberculin in the strengths used was found to produce a distinctly greater reaction than a 1:1,000 solution of old tuberculin. With TPT. 178 (96.2 per cent) of the positive reactors gave clear-cut positive tests while with OT. 166 (89.7 per cent) yielded positives. Thus with a dose 1 per cent as great, more positive reactors were detected with TPT. than with OT.

The dermotubin test yielded 152, or 82.1 per cent, of all positive reactors. This result is distinctly less favorable than that obtained by either intradermal method. The percentage, however, is much better than that yielded by the old Moro ointment (Ektebin), which in most

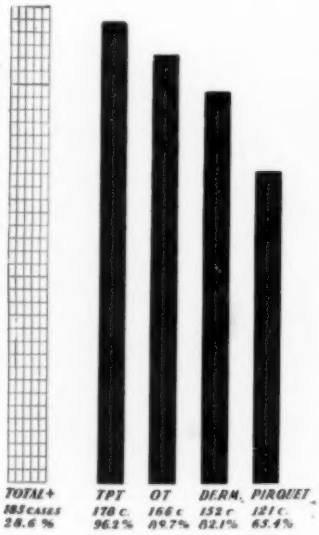

Chart 1.—Graph showing the relative proportion of total positive reactions yielded by each test.

investigators' hands gave about 50 to 60 per cent of positives. In our series it was also distinctly superior to the cutaneous reaction of von Pirquet, which yielded only 121 (65.4 per cent) of the total positives. Löwenstein quoted a number of workers who have used dermotubin in large series of cases. He stated that all agreed it was diagnostically equal to the Pirquet. Goldberg and Gasul[4] reported the results of 109 tests in which the dermotubin reaction was compared with the Moro, the Pirquet, and the Mantoux. Of these 39 per cent were positive to both the dermotubin and the Mantoux reactions, 36 per cent to the Pirquet, and 20 per cent to the Moro. These figures are not in agreement with our findings, the Mantoux with 0.1 mg. OT. being definitely superior to the dermotubin test. Kaan[5] found 94 per cent of tuberculous

individuals reacted positively to Löwenstein's ointment. Kundratitz[6] states that the dermotubin test, although a valuable diagnostic agent, is not as reliable as the intradermal reaction. Mändl[7] applied Löwenstein's ointment to sixty adults with tuberculosis and obtained a positive reaction in almost 100 per cent. Melion[8] found the percutaneous test, Ektebin or dermotubin, and the Pirquet test to be of equal value from a diagnostic standpoint.

There is considerable disagreement in the literature regarding the efficiency of the diagnostic Pirquet reaction. D'Arcy Hart[3] analyzed the results of forty-two authors who tested 4,787 cases of undoubted clinical tuberculosis. In this group the average error of the Pirquet test in the negative diagnosis of tuberculosis amounted to 16 per cent. When the cases were analyzed according to age, it was found that the error increased to 23 per cent among children. Hart stated that the Pirquet test as ordinarily performed is totally unsuitable for the negative diagnosis of tuberculosis. Wallgren[9] stated that the Pirquet test missed

Fig. 2.—Moderately positive Mantoux with TPT. 0.001 mg.

20 per cent of the individuals infected with tuberculosis, and that an intradermal test is absolutely indispensable to exclude scientifically tuberculous infection. Tisdall and Brown[10] tested 177 patients with both intracutaneous and scarification methods. They found 15.3 per cent gave negative reactions to the Mantoux 0.25 mg., while 41.9 per cent reacted negatively to the Pirquet. These authors stated that the intracutaneous test was infinitely superior to the Pirquet as ordinarily performed. In our series the scarification method of Pirquet yielded the poorest results of all. This was not dependent upon inferior tuberculin since the same material was used undiluted for the Pirquet as was used for the intradermal, the former giving 65.4 per cent of all positives and the latter approximately 90 per cent.

DISTRIBUTION OF THE POSITIVE REACTION

The children in this group of cases represent a special class of the population. They were all sick children; they were drawn from the poorer classes; they came principally from a relatively small area of the city; and they included a large percentage of colored children. For these

reasons the data given here are not directly comparable with similar statistics relative to the incidence of the positive tuberculin reaction in various urban populations. They are of interest, however, as an example of the incidence of the positive reaction in a hospital group. There are no published statistics regarding the distribution of positive reactors in Chicago. In other cities surveys have been made from time to time. Hart reviewed the literature on this phase of the problem completely. The findings twenty years ago in large European cities showed that at five years of age one-half the children reacted positively to tuberculin, at ten years about three-quarters, and at fifteen practically every child showed a positive reaction. Hetherington, McPhedran, Landis, and Opie[11] in a recent survey of school children in Philadelphia obtained figures only slightly below these. The averages obtained were 37.7 per cent at five years, and 90.2 per cent at eighteen years. In our group, although they represent a section of the population which should be most extensively tuberculized, the incidence of the positive reaction was far below these figures. In the group from two to five years of age 21.8 per cent reacted positively, five to ten years 25.7 per cent, and ten to fifteen years 47.7 per cent. Thus in the oldest group less than one-half showed positive reaction. (Table I.) When the races are separated, we find a very interesting difference in the incidence of the positive reaction. Two-thirds of these children were white and of these only 18.7 per cent yielded a positive reaction. On the contrary in the colored, practically all negro, 45.6 per cent of the entire group were positive. (Table II.) These figures indicate that of the children admitted to the Cook County Hospital, the number who have been infected with tuberculosis is about one-half that of the old European and recent Philadelphia series. Furthermore, the white children as a group are not at all extensively infected. Most of the positive reactions are contributed by the colored children, negro and Mexican, the incidence of infection being roughly two and one-half times as great as in the white. The geographic distribution confirms this finding and shows a very large number of positive reactors coming from the negro districts of the south side. Although we are dealing with a special section of the population, the figures are very striking; they indicate that while the spread of

TABLE II

DISTRIBUTION OF THE TUBERCULIN REACTION ACCORDING TO RACE

	NEGATIVE		POSITIVE		TOTAL	
RACE	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Colored	132	54.4	109	45.6	241	32.6
Negro	118	54.9	97	45.1	215	
Mexican	13	52.0	12	48.0	25	
Filipino	1		0		1	
White	330	81.3	76	18.7	406	67.4

tuberculous infection is apparently not great on our white population, an important source of infection is still present in our colored districts.

COMMENT

The selection of the most desirable technic in the performance of the diagnostic tuberculin reaction for routine office or hospital use is of great importance, particularly in pediatric practice. Several considerations must be met. First and most important, the test should be sufficiently sensitive to detect a high percentage of infected individuals. There are also secondary considerations, which are of importance to the practitioner. The test should be easy of application, should not require extensive preparation, and should be as painless as possible. It is obvious that the primary consideration is best met by the intradermal test. It may be carried out with a high degree of accuracy in dosages, free from danger of undesirable local or general reactions. The test requires some special training in its application, requires preparation in making dilutions and sterilization of syringes and needles, and is undoubtedly painful. Sensitive children are often much upset by the extensive preparations, and the somewhat elaborate technic excites comment from the parents, usually necessitating lengthy explanations of just what the test signifies. Many individuals are badly frightened by the statement, "a test for tuberculous infection," and the stormy reaction of the parents to such explanation often precludes the routine use of a test which otherwise might well be employed as a part of each office examination. In hospital practice, however, these objects are usually unimportant. It is our belief that the intradermal reaction using 0.001 mg. TPT. or 0.1 mg. OT. should be used as a routine in all children's hospitals to the exclusion of any other method. In this way a very high percentage of all positive reactors will be detected on admission, and, in the few negative reactors where the diagnosis is still in doubt, subsequent intradermal tests with stronger solutions of either of these materials may be employed. In the strengths used, vesicular reactions were occasionally obtained in hypersensitive individuals but bad sloughs or focal or general reactions were not seen.

The dermotubin test, while it does not fulfill the requirement of accuracy to the extent of the intradermal, is still a fairly sensitive test. Its great value lies in the ease and painlessness of application, which makes it most desirable for routine office use. A drop of ointment may be rubbed into the skin very casually without exciting any comment from either the mother or child. The test is so simple that it may also be used in the routine preparation of children by nurses where tuberculin tests are desirable, but the time of a medical attendent is not available at all times, as in health centers of various sorts. Though there may be some objection to nurses carrying out such procedures, there is so little possibility of injury that such a routine might be employed safely. By its widespread use many positive reactors might be detected even in re-

mote communities, and thus sources of infection discovered. The only objection to the test is that the material, not manufactured in America, must be imported, with the result of increased cost.

The distribution of positive reactors in the Cook County Hospital children is of interest because of the general low incidence of positives and the very low percentage of white children infected. These figures, while not the result of a complete survey of well children, are encouraging since they seem to indicate progress in the control of the spread of tuberculous infection. The negro group, however, is still heavily infected, and the colored districts are a source of danger since much open tuberculosis must be present in these areas. The tuberculosis morbidity in Cook County Children's Hospital confirms the results of the tuberculin tests. A total of 3,099 children were admitted to the medical wards in 1932. In this number were 110 cases of clinical tuberculosis. Of these sixty-four, or 58.1 per cent, died, nine were discharged unimproved, twenty-six were discharged improved, and eleven remained in the hospital chronically ill. About 80 per cent of these cases were colored children.

CONCLUSIONS

1. The intradermal reaction is best suited for routine hospital use and should supplant other methods for this purpose.

2. Total protein tuberculin (TPT. Seibert) is extremely sensitive and will detect a higher percentage of positive reactors than old tuberculin in doses one hundred times as great.

3. The dermotubin test, less sensitive than the intradermal test, is extremely useful because of the ease and painlessness of its application. It is well suited to routine office use.

4. The Pirquet scarification reaction is greatly inferior to either the intradermal or dermotubin test. Either of the latter are therefore preferable for routine use.

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BRUCELLA INFECTION IN CHILDREN

Agglutination Reactions and Intracutaneous Tests

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DESPITE the fact that *Brucella* infection (undulant or Malta fever), in adults has been increasing in the United States during the past ten years, comparatively few cases have been found in children. The usual method of infection in children is by drinking raw milk containing Brucella organisms, and considering the widespread distribution of *Brucella abortus* infection among the cattle of the United States, it is remarkable that so few cases occur. This situation is in part explained by the low pathogenicity of the average organism, pasteurization of milk, and the difficulty with which the human can be infected with this organism by way of the alimentary tract. It is possible that children may become immune, as a result of ingesting the organisms in raw milk, without having clinical infection.

Evidence of apparent immunity is suggested by the results of a study of a group of children, inmates of an orphanage, who, until October, 1931, were drinking milk infected with Brucella organisms of relatively low virulence. Attention was called to this situation by the occurrence of two typical cases of the disease in the institution, in a boy, nine, and in a girl, four years old.[1] The organism was isolated from the blood of both patients on several occasions, and, through the courtesy of Dr. Theobald Smith, was identified as a porcine strain of low virulence. Contagious abortion had been present for the past ten years in the herd supplying milk to the orphanage. Twelve of eighty-seven cows were found to have agglutinins in their blood serums, and these were removed by October 15, 1931. Serums from fifteen of a herd of seventy-five hogs were tested, with negative results. None of the children in the orphanage had contact with the animals, or with raw meat products, but all were drinking at least a pint of raw milk daily. Agglutination reactions and intracutaneous tests were made on 210 children in the orphanage, between four and fifteen years of age, who had been drinking infected milk for at least five months—some for as long as six years. They were closely supervised and were hospitalized for the slightest illness, or if the mouth temperature was above 37.3° C. None of them had, at any time while in the orphanage, illnesses resembling Brucella infection.

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Agglutination Reactions: The agglutination tests were made with four antigens of turbidity corresponding to the 1:4,000 U. S. Public Health Silica Standard: O, the organism isolated from the blood of the two patients with the disease; P, a virulent porcine organism; B, a bovine organism, strain No. 456 of the U. S. Hygienic Laboratory; and C, a caprine organism, strain No. 428 of the Hygienic Laboratory. The serums were in dilutions of 1:20 to 1:640. The tubes were placed in a water-bath for one hour at 37° C., left in the ice box overnight, and read at the end of twenty-four hours, in a uniform light. When the results were indefinite, or the controls positive, the tests were repeated. Table I is a record of the agglutination tests done on forty-eight children tested three weeks after they had stopped drinking infected milk; seven were positive, although none of them had ever had symptoms of Brucella infection. When tested two months later, these seven children had lost their agglutinins. A second group of 164 children in the institution was tested between November 24, 1931, and January 8, 1932, six to twelve weeks after they had ceased drinking infected milk, and none of them showed agglutinins.

Intracutaneous tests were done with a heat-killed saline bacterial suspension of the O strain, isolated from the active cases in the institution, and standardized by comparison of turbidity with the 1:1,000 U. S. Public Health Silica Standard. As a 1:15 dilution of this standard caused a marked reaction in the skin of the two patients who had recovered from the disease, 0.1 c.c. of this dilution was used for the tests. A definite erythema, 1 cm. in diameter, persisting for at least forty-eight hours was considered a positive test. Those children who had positive tests had larger reactions when a 1:5 dilution was used.

Table II shows the results of the intracutaneous tests done on 210 children. Twenty-seven, or 13 per cent, were definitely positive; six, or 3 per cent, had questionable reactions. The children who had positive reactions and an equal number who did not react were tested with strain No. 456, and the reactions were identical with those obtained with the O strain. The thirty-three reactors were tested several times between June, 1932, and April, 1933, and on the latter date, twenty months after the infected milk was discontinued, twenty-six of them still reacted in the same degree, and seven had become negative. However, only two of these seven were definitely positive when first tested. The twenty-six controls were infants in another institution, who were from three to eighteen months of age, and who from birth had been fed evaporated milk. None of them had positive tests.

DISCUSSION

Apparently it is possible for children to develop agglutinins for Brucella organisms without having a clinical infection, as suggested by the fact that seven of the first forty-eight children examined (14.6 per

cent) had agglutinins in their blood. Larson and Sedgwick[2] found that 17 per cent of 425 institutional children who were ingesting *Brucella abortus* in milk had positive complement fixation tests, and that the agglutination test paralleled the complement fixation test. Deitrich and Bonynge[3] found only one positive agglutination test among 1,000 children in the vicinity of Los Angeles; this child had been drinking raw milk on a farm in Kansas. Apparently, it is necessary to ingest fairly large numbers of organisms over a considerable period of time in order to form agglutinins without clinical evidence of the disease. Furthermore, the agglutinins tend to disappear rapidly when the infected milk is discontinued, for the seven children who had agglutinins had lost them within two months, and in the second group of 164 children under the same conditions, tested from six to twelve weeks later, no agglutinins were found. Agglutinins formed during a clinical infection, disappear rapidly during convalescence. Occasional cases of *Brucella* infection in which no agglutinins were present during the disease have been reported. We have seen two such cases in children.[1]

TABLE I

AGGLUTINATION REACTIONS OF FORTY-EIGHT CHILDREN THREE WEEKS AFTER THEY HAD CEASED DRINKING RAW MILK INFECTED WITH BRUCELLA MELITENSIS, VARIETY SUIS

CASE NO.	AGE IN YEARS	DURATION CONTACT	ANTIGEN*	AGGLUTINATION TITER			INTRACUTANEOUS TESTS	
				11/5/31	11/24/31	1/8/32	6/21/32	3/23/33
10	5	2 yr.	O	1:80	0	0	++++	++++
			P	1:160	0	0		
12	6	4 yr.	O	control	1:640	0	++	?
			P	pos.	1:160	0		
19	6	3 yr.	O	1:320	0	0	++	++++
			P	1:80	0	0		
26	6	5 mo.	O	1:160	0	0	+++	++++
			P	0	1:640	0		
27	6	18 mo.	O	1:640	1:160	0	++	++++
			P	1:640	0	0		
			B	1:160	1:160	0		
			C	1:80	0	0		
28	6	2 yr.	O	1:320	0	0	+++	?
			P	1:320	1:640	0		
48	15	6 yr.	O	1:160	0	0	+++	+++
			P	1:640	0	0		
Remaining 41 of the 48	5-15	4 mo. to 6 yr.	O	0			5 children +++	5 children +++
			P	0				
			B	0				
			C	0				

*O, strain isolated from cases at Orphanage.
P, virulent porcine strain.
B, strain 456, U. S. Hygienic Laboratory.
C, strain 428 U. S. Hygienic Laboratory.

The intracutaneous test should be read at both forty-eight and seventy-two hours, as the time of maximal reaction varies with the individual child. Thus, some reactions that are markedly positive

TABLE II

INTRACUTANEOUS REACTIONS (BRUCELLA)

SOURCE OF MILK	POSITIVE	QUESTIONABLE	NEGATIVE
Infected herd	27	6	177
Evaporated milk	0	0	26

with edema and swelling at forty-eight hours may show only a small papule at seventy-two hours. In this series in which 320 intracutaneous tests were done on 210 children, no reaction reached its maximum later than seventy-two hours after injection. In many of the children with marked reactions, a small papule remained, and was present for several months. In no case, with the dilution used, did necrosis occur, although four children had slight fever (37.8° C.) on the day following the injection. Leavell and Amoss,[4] and other workers,[5, 6, 7, 8] have found that a saline bacterial suspension gives more accurate results than filtrates or extracts of the Brucella organisms. Apparently any virulent Brucella organism can be used for the test. Care must be taken not to use too heavy a suspension, as a necrotic papule may form; lymphangitis (sterile) has been reported,[8] and general reactions often occur. A dilute suspension gives equally good results. The average ward patient is not a suitable control for the intracutaneous test, as he may have been in contact with Brucella organisms and, therefore, may react positively.

A positive intracutaneous test means active clinical infection, previous infection, or contact with the organism without clinical infection. On the other hand, despite statements to the contrary,[10] a negative test does not rule out active infection, for we have seen a child who had had the disease for eighteen months and yet intracutaneous tests with his own organism, and with strain No. 456 were negative.[1]

CONCLUSIONS

In a group of 210 children drinking milk infected with *Brucella melitensis*, variety *suis*, of low virulence:

1. Two developed the disease.

2. Fourteen and six-tenths per cent of the 48 tested early had agglutinins without clinical evidence of the disease.

3. The agglutinins disappeared rapidly when the infected milk was withdrawn.

4. None of the 164 tested several weeks later had agglutinins.

5. Thirteen per cent of the 210 had positive intracutaneous reactions.

6. When strongly positive, this reaction persisted for at least fourteen months.

7. A positive intracutaneous reaction indicates the ingestion of some

variety of *Brucella melitensis* at previous date, but not necessarily a clinical infection.

8. A negative intracutaneous test, as well as a negative agglutination test, does not eliminate the possibility of a clinical infection.

9. Normal infants who have not received infected milk do not have positive intracutaneous tests.

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DUKE HOSPITAL

Pediatric Clinics

THE BABIES HOSPITAL AND DEPARTMENT OF DISEASES OF CHILDREN, COLUMBIA UNIVERSITY, NEW YORK

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A DESCRIPTION of the pediatric clinic of Columbia University College of Physicians and Surgeons must be prefaced by two definitions. First, in the university organization the department is known as the Department of Diseases of Children; but the scope of the department extends to cover health as well as disease in children, as implied in the word "pediatrics." Second, the center of clinical facilities for the department is the Babies Hospital of the city of New York; the upper age limit of thirteen years signifies, however, that children as well as infants are admitted.

The departmental staff includes eleven full-time members, not including hospital internes and residents, and about fifty part-time physicians. All of the full-time staff are engaged in investigative work, some of it in clinical fields, others in the laboratories or in combined clinical and laboratory studies. A portion of the part-time staff has supervision of a ward from time to time, alternating with out-patient work; others confine their work to the out-patient department. The staff, as so described, includes the pediatric staff of St. Luke's Hospital and St. Mary's Hospital for Children, where elective courses for undergraduate students are given.

The research projects now actively under way include studies of the mechanism of formation and relief of edema, cholesterol metabolism and various clinical disturbances associated with its abnormalities, calcium and phosphorus metabolism in connection with certain bone diseases and disturbances of growth, the utilization of galactose in young individuals, factors influencing the osmotic pressure of the blood, the relationship of the hemolytic streptococcus to nephritis, the bacterial flora of the intestinal tract in early life with particular reference to the significance of bifidus organisms, and the classification and treatment of various forms of anemia. Under the supervision of the department of neurology, an investigation is being made of differential behavior patterns in normal children under the influence of a controlled environment, with special emphasis on the psychic and neuromuscular development of twins.

The Babies Hospital, which constitutes the pediatric division of the Presbyterian Hospital, has an active bed capacity of 152 beds, including fifteen private rooms and a semiprivate ward of twelve beds. These are divided among six floors as follows:

Infants' medical, up to 18 months;
Run-about medical, 18 months to 5 years;
Children's medical, 5 to 13 years;
Surgical;
Ear, nose, and throat;
Private floor.

The hospital has its own surgical operating rooms, its pathologic laboratory for postmortem examination and surgical diagnosis, its bacteriologic and chemical laboratories, and, of course, the usual clinical laboratory facilities. It also has its own x-ray unit. Equipped for the admission of all types of disease in children, it is operated in actual practice with a fairly rapid turnover, patients with chronic illnesses requiring long hospital care, such as tuberculosis of bone, being sent out to other institutions, so that the facilities of the Babies Hospital are directed mainly at diagnosis and the treatment of acute conditions. Facilities are not ordinarily available for the treatment of the communicable diseases, such as measles, diphtheria, and scarlet fever, for which the Department of Health requires strict isolation although during times of a widespread epidemic like that of poliomyelitis in 1931 an entire ward floor has been turned over to patients with the one disease. It is also feasible to retain a patient with a communicable disease by providing special nursing

The Babies Hospital
Columbia-Presbyterian Hospital Medical Center, New York City

care; this, however, is seldom resorted to because of the excessive cost of nursing service required. The average number of hospital admissions per year during the last four years has been about 2,150, involving approximately 35,000 hospital days' treatment per annum.

The out-patient department of the hospital is the pediatric section of the Vanderbilt Clinic, a separate building connected with the Babies Hospital by a covered bridge at the clinic floor level. The pediatric out-patient clinic is staffed by a full-time director and a working staff of internes from the Babies Hospital, practitioners volunteering for clinic service and, during the school year, to some extent by fourth-year students under faculty supervision. About 5,800 new patients are seen each year, the total visits per annum amounting to approximately 36,000. These figures apply to the general clinic, which is held every afternoon except Saturday, Sunday, and holidays. Special clinics, operated mainly in the mornings, are devoted to the following studies:

Allergy,
Anemia,
Cardiac disease,
Celiac disease,
Child guidance,
Congenital abnormalities and birth injuries,
Diabetes,
Epilepsy,
Medical follow-up,
Neurologic follow-up,
Nephritis,
Premature follow-up,
Surgical follow-up, and
Tuberculosis.

Columbia-Presbyterian Hospital Medical Center
Babies Hospital in Right Foreground

The Babies Hospital visiting staff also supervises the nurseries for newborn infants and the premature service of the Sloane Hospital for Women, the obstetrical component of the Columbia-Presbyterian Hospital Medical Center.

The interne staff of the Babies Hospital consists of a resident and one assistant resident, each on service for one year, and nine internes on service for eighteen months. The interne services commence on the first of January and the first of July, and each interne has two months on each of the clinic floors listed above and, in addition, on pathologic laboratory service, Sloane newborn service, and on admitting duty, comprising in all, nine different types of pediatric experience. Both the resident and the assistant resident receive a small salary in addition to board, lodging and laundry; the internes receive no separate salary.

Staff conferences are held once a week during the school year, at which problems of clinical and of scientific interest to pediatricians are set forth and discussed, and at which visiting physicians and medical students are welcome. Other scheduled exercises include a monthly clinicopathologic conference, semimonthly x-ray conferences, and the monthly meeting of the journal club; and each week at history meeting, the clinical records of the most interesting or significant cases discharged within the past week are reviewed by the interne and resident staff, the physician-in-chief, and a group of attending physicians.

The School of Nursing provides a three-month course in pediatric nursing to forty-eight undergraduate students from seven affiliating hospitals, a six-month course to four postgraduate students and a one-year course for fifteen infants' nurses. Each ward floor is in direct charge of a graduate nurse and one or two graduate assistants; in addition, the private floor nursing staff comprises graduate nurses exclusively.

The undergraduate course in diseases of children at the College of Physicians and Surgeons comprises, in the third year, 20 lecture hours, 20 discussion hours, and 12 hospital hours (the last mentioned in communicable diseases only); in the fourth year, 10 lecture hours, 30 clinical demonstrations and 18½ days of practical ward and out-patient service—a total of 203 hours. The 12 hours assigned to the study of communicable diseases take the student to the Willard Parker Hospital; the rest of the required time is spent at the Babies Hospital or in the out-patient clinic. Additional elective courses during the third year are given at St. Luke's Hospital under the supervision of Dr. F. Elmer Johnson and at St. Mary's Hospital for Children under Dr. Dever S. Byard.

Graduate physicians applying for a short course in pediatrics are customarily referred to the service of Dr. Roger H. Dennett at the Postgraduate Hospital and Medical School. Physicians approaching the study of pediatrics with the intention of equipping themselves as specialists in this field may offer themselves as candidates for the degree of D. Med. Sc., for which an intensive course is planned, comprising three years' work at the Babies Hospital and allied institutions of the Medical Center.

The facility with which the resources of the other departments of the center may be utilized is an important factor both in the study of our more obscure pediatric problems and in our efforts in the field of pure research. It might be stated in summary that the Columbia-Babies Hospital unit aims at a balanced grasp of its threefold opportunity in teaching, in clinical service to the community, and in investigation.

630 West One Hundred Sixty-Eighth Street

Critical Review

ALLERGIC DISEASES

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WITH this year's review of allergic diseases, a certain amount of overlapping was unavoidable. The reviewer has tried, however, to eliminate repetition by referring to his previous discussion[1] where special phases of the subject were given more extensive treatment.

Progress was made along all lines, but 1933 did not keep up with the preceding four years in the publication of noteworthy books on allergy. *Allergy and Immunity in Ophthalmology*,[2] a monograph by Woods was the most outstanding piece of work. The book gave a very good statement of the present knowledge of allergy in its many phases and directed particular attention to the peculiarities of structure and reaction of the eye. *Some Thoughts on Asthma*[3] by Cameron and Coke's *Colds and Hay Fever*,[4] British publications, were not available.

Feinberg's[5] manual dealing with *Asthma, Hay Fever and Related Disorders* may well be compared with Joslin's *Manual for Diabetic Patients*. Although large clinics may have certain written forms of instruction for patients, this book fills a definite need in eliciting cooperation from intelligent patients, and covers the field concisely and authoritatively. It might have been made more useful if a few recipes for egg-free, wheat-free and milk-free foods were included.

GENERAL CONSIDERATIONS AND CONSTITUTIONAL STUDIES

Rackemann[6] and his coworkers have continued to study the allergic constitution, and have found that agglutinin development (to typhoid) in a group of allergic individuals was lower than that found in a control group. The difference between the two groups was, however, not great. In contrast with McConnell,[7] they found that the response of the skin in the allergic group was greater when tested with histamin than was the response in the control group.

Nelson,[8] studying the allergic constitution, reported the predominance of this state in males in the first decade and in females in the second and third decades.

A short discussion of the asthmatic state and the rôle of varied stimuli made the paper by Baldwin[9] very interesting. The symptom-complex of asthma may have various causes, but the allergic is foremost, as is shown in the study of any group of asthmatic patients, and fortification of stimuli may then be a frequent occurrence.

Topper and Mulier[10] in a study of the basal metabolism of twenty-five cases of asthma and twenty-five cases of epilepsy, found the rates for these conditions in the lower limits of the normal rates. Their interpre-

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tation of reduced thyroid secretion by exhausting episodes seems unwarranted in view of the known variabilities of the method and the slight differences they obtained.

Accepting migraine as a symptom-complex, Rinkel,[11] in a comprehensive and convincing discussion, cast considerable doubt on the assumption that it is easily accounted for on an allergic basis. The reviewer feels that such reports are of the greatest value in checking the overenthusiastic statements of the past.

Adamson and Sellers[12] in a less conservative discussion based, however, on a statistical study of the history and skin test, found a brief for the rôle of hypersensitivity in epilepsy.

It would seem that adequate control statistics are difficult to evaluate. Vaughan's[13] report on minor allergy suggested that while 10 per cent of the general population may have major allergic manifestations, fully 50 per cent may have minor episodic symptoms, which incidence speaks for a quantitative rather than a qualitative difference between the allergic and the normal individual; that the allergic response is only "an exaggeration of the physiologic response."

Rich,[14] in discussing the allergic response in bacterial allergy, took issue with the accepted theory that allergy is a phase or step in immunity and emphasized the harmful aspects of allergy which, he believed, should be avoided as they are not beneficial but, in all likelihood, injurious.

Among the British reports is a discussion by Burn,[15] who suggested that asthma may be related to a deficiency of adrenal secretion. The idea is attractive from a theoretical viewpoint. Waldbott,[16, 17, 18] in this country, made similar implications in his discussion of the relationship of status lymphaticus to allergy when he suggested that an anaphylactic edema of the lungs might be the cause of sudden death; in such instances hypoplasia of the adrenals was a frequent pathologic finding. So far as thymic enlargement is concerned, the reviewer feels that Boyd's[19] work has cast considerable doubt on its significance. The possibility of functional hypoadrenalism in allergy, however, might well be studied. Isolated instances with which the reviewer is familiar suggest that the benefit from insulin therapy may be interpreted as possible adrenal stimulation. The study of chloride, sodium, and potassium partition such as Loeb[20] applied to Addison's disease has not, to the reviewer's knowledge, been applied to allergy.

Fineman[21] has reported the use of suprarenal cortex extract in the treatment of bronchial asthma, but he followed only the blood pressure, weight, pulse, etc. His results, while not striking, warrant further studies. It is the opinion of the reviewer that while endocrine therapy has been disappointing in the past, the newer methods of hormone isolation may yet reveal some fractions, other than epinephrin, which will prove of value.

In several reports American investigators[22, 23] have failed to substantiate the findings of Oriel and Barber[24] regarding the specific urinary proteose. Westcott and Spain[25] have studied the sedimentation rate of erythrocytes in allergy. They found the rate within normal limits in pure allergic conditions, but more rapid than normal in conditions complicated by infection. Similar conclusions were made by Uffe.[26]

DIAGNOSIS AND TECHNIC

Alexander[27] has made a brief survey of the methods used by various specialists in allergy in the United States and Canada. One is struck by the diversity of methods though there seems to be developing an agreement as to preferred routines. The efforts of the Society for the Study of Asthma and Allied Conditions to obtain standard terms and methods, etc., are interesting. Berkoff[28] described a standard for measuring skin reactions. The method may be of value in the study of small groups of cases, but it is impractical for wholesale adoption. Rowe[29] has reiterated the fallibility of the skin tests, especially to foods, and explained the value of his elimination diets. In contrast, Stewart[30] believed that, even granting the variability in technic and interpretation, the skin test remains of great value when intimate studies of the patient and the history are made. In these instances, the elimination diets are of secondary importance. Alles, Piness, and Miller[31] reported the stability of some food allergen extracts for as long as seven years. Preservation was by storage in a cold atmosphere.

Rappaport[32] has shown that ragweed pollen extracts may be preserved by concentration of the extract by drying at 40° C. From such concentrates dilutions may be made whose potency seems proportional to their nitrogen content. Extracts of pollen using 50 per cent glycerin are reported by Brown[33] as giving better results in treatment than those obtained with weaker glycerin or aqueous solutions.

An interesting discussion in the Society Transactions,[34] which gives more detail, concerns the method of standardization of pollen extracts as advocated by Cooke and his coworkers (Cooke, Vander Veer and Barnard,[35] and Cooke and Stull[36]). Coca[37] contends that the method of determining total nitrogen content is not open to the criticism that obtains for the method of phosphotungstic (albumin nitrogen) precipitation.

It will be recalled that opinion is divided regarding the effect of treatment on the intensity of the skin test. Markow and Spain[38] reported a lessening of the cutaneous reaction after long therapy. Colmes and Rackemann[39] likewise found a decreased skin-test reaction in the majority of cases regardless of the number of therapeutic injections. They did not feel that this was parallel with the clinical response or that it might be used as a gauge of therapeusis.

Cromwell and Moore,[40] reported further immunologic relationships in extracts of short and giant ragweed pollen. By use of their trypan blue skin test for rabbits they concluded that the antigenic structures of these closely related pollens are different. With Unger,[41] these investigators repeated Black's work on the polysaccharid fraction and the purified protein fraction of Stull, Cooke, and Chobot. They concluded from their animal and human studies that the protein fraction was essential while the polysaccharid played no specific part. The work of Vallery-Radot and his coworkers[42] may well be mentioned here. His tests with root, stamen, and pollen extracts showed some relationship but still emphasized the specificity of the pollen fraction. Hence it would seem that allergens as exemplified by pollens showed extreme specificity even though related botanically and even though possessing some fractions in common.

Concerning passive transfer studies, the work of Lichtenstein[43] is inter-

esting. He was able by drying to preserve sensitizing serum for from six to fourteen months. While there was some diminution of skin sensitizing power, the redissolved serum was still potent. A toxic factor, as judged by the skin response on injecting the serum after six months' preservation, was noted. This may be due to a change comparable with that which occurs in undried serums after twelve days' refrigeration. Walzer[44] described a nonspecific cutaneous sensitivity which is passively transferable to normal skins. While Walzer stressed it as an indication for the necessity of control of Prausnitz-Küstner reactions, the phenomenon suggests to the reviewer that it may also be considered an evidence of the transfer of hypersensitivity to trauma.

BACTERIAL ALLERGY

Reports in the field of bacterial allergy, although numerous, lead the reader to question the efficacy of the ordinary methods of allergy study such as the skin test, etc. Caulfeild[45] has reviewed some of the recent advances in bacteriology which might be expected to contribute to this clinical problem. Along this line, Benson[46] reported a study of skin tests made with extracts of gram-positive cocci from normal and abnormal intestinal flora. He used extracts from both "R" and "S" types, finding little difference with regard to the skin response. "O" types gave a stronger reaction than "H." The finding of positive skin responses in nearly all patients (and controls) and the fact that ricinoleated extracts were inert suggest a toxic response not altogether specific. It is possible that dilution of the bacterial allergen may diminish the general response leaving a more clearly cut picture of specificity. It is appropriate to mention the discussion of Benson's paper which appeared in the Society Proceedings,[47] where Cohen aptly called attention to the fact that the diagnosis of bacterial allergy, because of failure of common skin tests, etc., is open to considerable criticism, and also to the fact that bacterial allergy is still difficult to compare with the usual forms. Thomas and Touart[48] described a late skin reaction to vaccine, which they considered a specific bacterial allergic response. They discussed its significance in relation to the selection of the vaccine for treatment, the dosage, and the time factor in administration. This delayed skin reaction resembles the so-called "patch" test used in dermatitis. The reviewer wonders if patch tests with bacterial products would be of any particular value. Delayed response is quite characteristic of the tuberculin and Dick tests; and an ointment tape test for tuberculosis has proved most reliable in Wolff's[49] study. Wilmer and Cobe[50] were enthusiastic about results from selective vaccines. They found that a selection of organisms, somewhat as pollens are selected for the hay fever patient, is preferable to the use of the nonspecific stock and autogenous vaccines.

It is not within the scope of this review to report the numerous studies in the field of bacteriology. It is sufficient to say that clinical studies may be ill advised unless competent bacteriologic supervision is obtained. After the confusion of reports regarding the many factors in the problem of bacterial allergy, the clinical discussion of Lintz[51] is refreshing. He reported benefit in intractable asthma by sterile abscess formation. Such obvious nonspecific therapy (immune mechanism shock) followed by improvement makes one question the reports on specific bacterial fractions.

DERMATOSIS

Many dermatoses due to cosmetics are well known. During the past year considerable attention has been directed to eyelash cosmetics (Lashlure, etc.). Widespread interest may have been excited by the recent publicity given by Mrs. Roosevelt to the dangers of these preparations. An excellent review of the rôle of cosmetics is that by Hollander.[52]

Sulzberger and Kerr[53] in discussing eczematous sensitization presented ten case studies in which the usual skin test was of no value while the patch test was very helpful. They found the patch test of exclusive value in occupational dermatoses, and they showed that the zones of clinical involvement were the most sensitive to the test. Sulzberger and his coworkers[54] also claimed that silk sensitivity is often found by test but that its significance, clinically, in dermatosis is open to question. Figley and Parkhurst[55] refuted this claim by reporting five instances of eczema, with silk sensitivity of major consideration, in which the patch test was negative and the skin test positive. The occurrence of respiratory symptoms also suggested to them that in many instances silk might act as an inhalant rather than a contact excitant. Taub and Zakon[56] likewise took issue with Sulzberger regarding the significance of silk reactions. Their cases had further study by passive transfer.

Greenhouse and Sulzberger[57] reported dermatitis from the common weed, tansy. As before, they reported negative skin tests but positive patch tests, and overdosage orally gave an acute skin response. A very interesting study of *Rhus toxicodendron* poisoning was that of Gowen.[58] It is strange, however, that no mention of the work in this field, which the reviewer feels is fundamental, was made by McNair.[59] Gowen reported excellent results both therapeutically and practically with the single intramuscular injection of the rhus extract in almond oil. No doubt this method will prove of great value in the treatment of similar (alcohol-soluble) plant fractions. Harville[60] found an alcohol-soluble fraction from the garden plant "bleeding heart" responsible for a dermatitis. Abramowitz and Noun[61] described a dermatitis from chloral.

In the more general field of allergy, acacia has again been reported by Spielman and Baldwin.[62] Watson and Kibler[63] attributed an instance of asthma to drinking water. Chlorination was held responsible by them for the action of the water, though salt used on the patient's food was innocuous. Discussion of this paper by Phillips[64] suggests that other factors may be involved. He referred to an instance of coal tar sensitivity in which oil used on the water pumps was the important vehicle. Harkavy,[65] interested in the rôle of tobacco in thromboangiitis obliterans, found a preponderant number of positive skin tests in smokers with thromboangiitis obliterans in contrast with smokers without this disease. The latter group, however, gave a greater incidence of skin reactions than the nonsmoking controls.

Kern and Schenck[66] showed allergy to be an almost predictable factor in the etiology of mucous nasal polyps. Their study was careful and convincing. Bullen[67] found the incidence of asthma in 400 cases of chronic sinusitis insufficient to incriminate the latter as a causal factor. His statistics for chronic bronchitis and bronchiectasis supported the same conclusion with regard to their etiology. It is the reviewer's opinion that in the past there has been an overemphasis on sinusitis as a cause of asthma. Sinusitis might occur secondarily as a result, not a cause, of edema of the nasal mucosa which prevents normal sinus com-

munications; and many times the operative preparation (cocainizing of nasal mucosa) for sinus drainage may relieve a coincidental asthma. The latter phenomenon seemed a probable factor in the results obtained by Spivacke.[68] His treatment of vasomotor rhinitis by painting the nasal wall with carbolic acid was followed by relief in ten out of sixteen patients. The treatment would seem not altogether free from hazard. Similarly, the treatment by Swineford and Weinberg[69] of a heat-sensitive patient with vaccine appeared very courageous. It would seem that graded exposure to heat might well be tried before intravenous vaccine, even admitting the beneficial results from that preparation in chorea.

Shookhoff and Lieberman[70] mentioned a new symptom referable to allergy in the occurrence of angina pectoris in patients with acetylsalicylic acid sensitivity, as well as in a patient with ragweed pollinosis. Preexisting cardiovascular disease seemed, however, to be a necessary factor. Purpura in a malarial patient is described by Cazot.[71] While suggesting a type of allergic response to quinine, the report is not convincing.

In the study and treatment for inhalant excitants, Feinberg and Steinberg[72] found a variation in pollen potency with the season of collection. They also pointed out a lack of correlation between the pollen measure for ophthalmic and nasal tests when compared with the probable exposure measure for clinical response. Phillips[73] reported the satisfactory use of coseasonal intradermal pollen administration. Rappaport and Reed[74] found viosterol of therapeutic value in hay fever, but not in infectious asthma. Vaughan and Cooley[75] and Kahn and Grothaus[76] found the air-conditioned room of great value in inhalant sensitivity. The latter authors stressed the benefit in patients with negative skin tests. Lamson and Watry[77] have been making a detailed study of the botany and pollen factors along the Santa Fé Railroad in New Mexico and Arizona. Their reports, although complete, offer little except an explanation of a method which could be used in more populous districts. The Wodehouse[78] survey of Yonkers should prove of value because it is an analysis in a heavily populated district.

A new milk-, wheat-, and egg-free food for infants with eczema has been studied by Cohen and his associates.[79] It is suggestive of the liver soup mixture used by Park many years ago in New Haven. From a theoretical aspect it would seem preferable to Sobee, since this new preparation, Cemac (Mead Johnson and Company), has its source of protein from beef. It is usually assumed that animal protein is a better tissue builder than protein of vegetable origin, experience to the contrary nothwithstanding. Cohen's report of alleviation in the majority of patients fed with the preparation seemed a bit optimistic considering the multiplicity of factors which produce eczema. Nevertheless, Cemac should be a welcome addition to our armamentarium.

Peck and Salomon[80] presented an excellent discussion of eczema. They minimized the rôle of foods and emphasized contact excitants (such as feathers) and the patch test.[53] In the reviewer's hands the patch test in infants was unsatisfactory because of the heightened irritability of the infantile skin. Concerning the rôle of egg, which Peck and Salomon considered indicative only of the expected allergic constitution, the effect of feeding that food and its response to the patch test leave no doubt as to its specific importance.

In spite of progress obtained in recent years, allergy still presents many problems open to debate and offers an attractive experimental field for the investigator.

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American Academy of Pediatrics

Proceedings

REPORT OF THE COMMITTEE ON HOSPITALS AND DISPENSARIES

INTRODUCTION

Many phases of work of the recent White House Conference on Child Health and Protection have been taken up and quite energetically followed by medical and lay groups. The problem of the child in the hospital has received comparatively slight consideration. Appropriately the American Academy of Pediatrics has made a study of this subject. In order to make a satisfactory study of the problem, the Committee decided that it was necessary to have detailed information concerning the various children's hospitals in this country and Canada. Consequently, there was obtained from the American Medical Association, a complete list of the children's hospitals in these countries. Here we met our first difficulty. No one knew what could be strictly classified as a children's hospital. Several hospitals designated as children's hospitals were really tuberculosis sanatoriums or convalescent homes for children. Many of the so-called women's and children's hospitals were actually maternity hospitals in which the welfare of the child might be secondary in importance to the care of the mother. Several hospitals were excluded, which in themselves were children's hospitals, but were a part of a general hospital. The Committee finally after appealing to the membership of the Academy for advice as to whether certain hospitals could be classed as children's hospitals or merely as homes and sanatoriums, chose rather arbitrarily the hospitals in the group which is here being presented. We are relatively certain that the thirty-five hospitals in this group represent all the large, general children's hospitals in the United States and Canada and that they do not include orthopedic or hospitals for contagious diseases, convalescent homes for children, summer camps, or tuberculosis hospitals for children. An attempt, therefore, has been made, as far as possible, to limit this survey to a study of the general children's hospitals. The following is the list of hospitals finally agreed upon:

Children's Hospital, Los Angeles, Calif.
Hospital for Children, San Francisco, Calif.
Children's Hospital, Denver, Colo.
Children's Hospital, Washington, D. C.
Bobs Roberts Memorial Hospital, Chicago, Ill.
Children's Memorial Hospital, Chicago, Ill.
Sarah Morris Hospital, Chicago, Ill.
Cook County Hospital, Chicago, Ill.
James Whitcomb Riley Hospital, Indianapolis, Ind.
Children's Hospital, Iowa City, Iowa
Children's Hospital, Portland, Maine
Harriet Lane Hospital, Baltimore, Md.

Boston Floating Hospital, Boston, Mass.
Children's Hospital, Boston, Mass.
Children's Hospital, Detroit, Mich.
Children's University Hospital, Ann Arbor, Mich.
Children's Memorial Hospital, Kansas City, Mo.
St. Louis Children's Hospital, St. Louis, Mo.
Children's Hospital, Buffalo, N. Y.
Babies Hospital, New York, N. Y.
New York Foundling Hospital, New York, N. Y.
New York Nursery and Children's Hospital, New York, N. Y.
St. Mary's Hospital for Children, New York, N. Y.
Seaside Hospital, Staten Island, New York, N. Y.
Children's Hospital, Akron, Ohio
Children's Hospital, Cincinnati, Ohio
Babies and Children's Hospital, Cleveland, Ohio
Children's Hospital, Columbus, Ohio
Children's Hospital, Philadelphia, Pa.
Children's Hospital, Pittsburgh, Pa.
Children's Orthopedic Hospital, Seattle, Wash.
Milwaukee Children's Hospital, Milwaukee, Wis.
Montreal Children's Memorial Hospital, Montreal, Quebec, Canada
Toronto Hospital for Sick Children, Toronto, Ontario, Canada
Children's Hospital of Winnepeg, Winnepeg, Manitoba, Canada

Fully aware that the questionnaire method of obtaining information is not always entirely satisfactory, the Committee could think of no other way to approach the subject in a manner any way adequate. If one resorts to the impressions obtained by personal contact, he is often forced to accept opinion rather than facts. By dealing with the questionnaire method one obtains only facts. Often in dealing with institutions, impressions are of more value than facts, and occasionally, traditions are more valuable than either of these. However, the mere physical side of a hospital is not the only thing which can be examined by the questionnaire method. By this method much can be discovered of the way in which the hospital is run and something of the ideals forming the background of its administration. The final form of the questionnaire was largely due to the cooperation and advice of Dr. Philip Van Ingen who had so much experience with questionnaires of all kinds during the late White House Conference. After the questionnaire had been prepared and the hospitals chosen, each questionnaire was put in the hands of a member of the Academy associated with the particular hospital, with instructions that it was to be answered in detail. The task was carried out in every instance, and within four months all questionnaires had been answered and returned to the Committee. The Committee wishes to recognize this fine cooperation and to express its appreciation to these men.

After receiving and carefully tabulating the questionnaires, the various sections were separated and placed in the hands of experts in the respective fields, with the request that they criticise them. As we anticipated much of the material which these experts wished was not obtained.

The Committee did not feel that it was fair to ask of individuals directly connected with the particular hospital their opinions as to the efficiency, or lack of it, in that hospital. While many of these opinions might be eminently fair, there is always the possibility, and even the probability, that no matter how strong the good intentions of the individual may be, being human, he would have prejudices which would make it impossible to obtain an unbiased opinion. On the other hand, it is difficult for one coming from the outside to sense the place in the community which

the given institution holds, and therefore, the value of this opinion is impaired. We, therefore, concluded that the best we could do would be to gather facts and from these, so far as was possible, deduce some idea of the organization, efficiency, and personality of the particular hospital. The result has not been entirely satisfactory but much valuable information has been obtained as the present and subsequent articles will reveal.*

The Committee on Hospitals and Dispensaries of the American Academy of Pediatrics includes:

Dr. Clifford G. Grulee, Evanston, Ill., Chairman
Dr. George F. Munns, Winnetka, Ill., Secretary
Dr. Murray H. Bass, New York, N. Y.
Dr. L. R. DeBuys, New Orleans, La.
Dr. Roger H. Dennett, New York, N. Y.
Dr. Henry Dietrich, Los Angeles, Calif.
Dr. Lewis Webb Hill, Boston, Mass.

The Committee wishes to acknowledge the assistance given it by Dr. Bert W. Caldwell, Executive Secretary, American Hospital Association; Dr. Homer F. Sanger, Staff of the Council on Medical Education and Hospitals, American Medical Association; and Dr. G. Harvey Agnew, Secretary, Department of Hospital Service, Canadian Medical Association.

A. Professional Staff

1. *Attending Staff*

Since, as will be revealed later, nearly all the patients who go to children's hospitals are charity patients, it was not of so much importance to find out whether these hospitals had "open" or "closed" staffs. As a matter of fact, in twenty-one of the hospitals all patients in the wards came under the exclusive care of the attending staff. In two hospitals any accredited physician in good standing could send patients into the wards and treat them there. In twelve hospitals a limited number of physicians outside the attending staff could send patients to the wards, and in one instance, this privilege was extended only to outstanding specialists. In other hospitals this courtesy was extended to members of the associate staff or former staff members. In six hospitals the courtesy was extended only for pay patients. Table I will give some idea concerning the attending staffs in these hospitals.

It will be seen that in most instances the hospitals had provision for attending men in nearly every specialty which was needed although comparatively few hospitals have staffs in psychiatry and psychology. In most instances, provision was made for these services by other than attending men. Oral hygiene was frequently associated with dentistry, as was oral surgery. Since urology of children has taken such rapid strides within the last few years, it is surprising to know that only fourteen of the thirty-five hospitals have urologists. There were only nine of the hospitals that had any members on a full-time basis, and these apparently were only in the pediatric staff. Where it was possible to determine, it was interesting to see what a large proportion of the hospitals have attending men for the full twelve months of the year and how few have even comparatively unimportant branches on call only. The Committee feels that from one to three months is too short a time to serve efficiently on any service and that six months should be the minimum period of service. Something may be said for an attendance which takes in six months of the year, but very little for any attendance of less than that time. This survey of the hospital staffs does not, of course, bring out the regularity of

*Since the data for these reports were obtained one hospital has been closed and become part of a general hospital. The original figures, however, have been included in this report.

TABLE I

HOSPITAL ATTENDING STAFFS

	PEDIATRIC STAFF	OTOLARYNGOLOGY STAFF	ORTHOPEDICS STAFF	OPHTHALMOLOGY STAFF	SURGERY STAFF	NEUROLOGY STAFF	PSYCHIATRY STAFF*	PSYCHOLOGY STAFF†	DERMATOLOGY STAFF	DENTISTRY STAFF	ORAL SURGERY STAFF	ORAL HYGIENE STAFF	X-RAY STAFF	PATHOLOGY STAFF	ALLERGY STAFF	UROLOGY STAFF	CARDIOLOGY STAFF	DIABETES STAFF	BRONCHOSCOPY STAFF
Hospitals having	35	35	35	34	35	35	27	10	35	33	30	25	34	35	21	8	2	1	1
Total number of members	4-38	2-16	1-10	–	2-20	1-6	–	–	1-5	1-10	1-3	–	1-5	1-4	–	–	–	3	2
With full-time staff (1 or more)	9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Length of service in months	3-12	1-12	4-12	3-12	2-12	2-12	–	–	4-12	4-12	–	–	4-12	4-12	–	–	–	–	–
No. for 12 mo.	14	14	20	18	–	13	–	–	17	31	–	–	32	33	–	–	–	–	–
"On Call" only	0	0	6	8	2	7	5	7	7	6	3	–	4	4	12	6	–	–	–

*One hospital has facilities at Child Guidance Clinic; three combine Neurology and Psychiatry.
†Twelve other hospitals nave arrangements for psychologic work.

attendance nor the relative merits of the individuals employed. It is, of course, necessary for children's hospitals to take care of a larger number of pediatricians, than would otherwise be the case if the children's departments in general hospitals were more adequate. For this reason service of less than six months in some instances is thought to be necessary in order that all men on the staff may have an opportunity to work in the wards. A hospital service of less than six months would certainly not be of any great value to any one and, least of all, to the hospital. On the whole we may say that the evidence which is presented here concerning the attending staffs indicates that not only are the pediatric staffs adequate in number, but that there is a marked tendency to encourage the work of the other specialties in children's hospitals and to consult with these specialists.

2. *House Staff*

a. Residents

Only three of the thirty-five hospitals have no resident staff. One had as many as six; one, five; four, four; one, three; three, two; and twenty-one, one, making a total of fifty-seven. All hospitals which have residents pay them a salary; these salaries vary from twenty-five dollars to one hundred and fifty dollars per month. Women are eligible in two of the hospitals, and one hospital accepts only women as residents.

The length of service is one year in twenty-eight hospitals and varies from three months to two years in others. The qualifications for residents vary greatly. In sixteen hospitals one year of general interneship and one year of pediatric interneship are required while in five hospitals three or more years of general and pediatric interneship are required. Six hospitals require only one year of general interneship, and on hospital requires only "previous hospital experience." Two hospitals require one year of general interneship plus some pediatric experience. In contradistinction to these, one hospital required three years of pediatric interneship.

In only ten hospitals the resident does not have dispensary duties. The duties of a resident in the dispensary vary greatly in different hospitals and, in one only, is the resident in charge of the dispensary.

With respect to the resident, therefore, we see that there are provisions for fifty-seven residencies in the thirty-five pediatric hospitals of this country and Canada; that the salary varies from twenty-five dollars to one hundred and fifty dollars per month; that women are eligible to a large extent; and that the length of service in the average hospital is one year.

In view of the fact that the resident usually has considerable responsibility in the average hospital plan of pediatric care, it is gratifying to note that twenty hospitals require two or more years of previous hospital experience before a physician may qualify for that position.

We seriously question whether one year of general interneship properly prepares a man for a residency; we feel that the minimum requirement should be one year of general interneship and one year of pediatric interneship or assistant residency.

About one-third of the hospitals report that the resident has no dispensary duties. Undoubtedly dispensary service is a very valuable factor in training a young man for future work in pediatrics, and the resident should always have some duties there. Furthermore, his familiarity with the dispensary work will enable him to coordinate more efficiently the hospital and dispensary work.

b. Assistant Residents

Twenty-four hospitals have assistant residents. The number varies from one to eight, the total being seventy-two. In twenty of the twenty-four hospitals, assistant residents receive a salary and this varies between ten and eighty dollars per month. Women are eligible for this position in twenty-three of the hospitals,

and in one hospital they alone are accepted. The length of service varies from three months to one year, but in twenty of the twenty-four hospitals, the service is for one year. Qualifications for assistant residents are not quite so varying as those for residents. In fourteen hospitals one year general interneship is all that is required, while in nine, one year general and one year pediatric interneship. One hospital requires a year of general interneship with some pediatric training. In sixteen of these hospitals, the assistant resident has general duties in the dispensary, and in one he has optional duty.

We see, therefore, regarding assistant residents that there are places for seventy-two, which makes a grand total of one hundred and twenty-nine for residents and assistant residents; that the salary for assistant residents varies from ten dollars to eighty dollars per month; that the qualifications are in general, a general interneship or that plus a year's pediatric interneship; and that assistant residents are employed in dispensaries less often than are residents.

c. Internes

Thirty of the children's hospitals have internes. The number varies from one to fifteen; five have ten or more, ten have five to ten, fifteen have five or less. In all, these hospitals employ one hundred and eighty-four internes. Only eleven of the hospitals pay salaries to internes, and these vary from less than twenty-five dollars a month to forty dollars a month. In four hospitals are women ineligible, and in only one are men ineligible. The length of the interne services varies from six weeks to one year, but in nineteen of the thirty hospitals the service is for one year and in three for six months. In twenty-six of the hospitals, the service is rotating. The time on each varies from two to four months. The qualifications for internes vary. In ten hospitals only the M.D. degree is required, but in twelve a year's general interneship is necessary. In four hospitals the internes rotate through the children's hospital from a general hospital service. In all but three of the hospitals, the internes have general duties in the dispensary.

We see, therefore, that in all there are employed one hundred and eighty-four internes in thirty children's hospitals of this country and Canada. Presumably the other five hospitals have only residents. An interne service of less than six months can certainly be of no value and should be discarded. Happily the number of these is decidedly few. Of the one hundred and eighty-four interneships, sixty-two, or almost exactly one-third, have a service of less than one year. Dispensary duty is carried out in almost every instance, and we feel that this duty is a very valuable experience to all internes.

A general survey of the residents and internes will show that there are every year in the thirty-five children's hospitals, three hundred and thirteen internes and residents of which two hundred and fifty-one have at least one year's training, the other sixty-two being internes with less than a year's service. Of course, it is altogether likely that many of the residents and assistant residents come up from the ranks of internes, but since the residents and assistant residents constitute only one hundred and twenty-nine, the reduplication is not much. In all probability, we may say, that there are to be turned out each year in the neighborhood of two hundred men who have had at least a year's training as resident or interne in a children's hospital. This group alone would certainly be sufficient to replace all vacancies in the pediatric profession caused by death, illness, etc., and would leave a large number for influence on general practice or other specialties.

d. Educational Activities

Some idea of the value of a hospital may be obtained by inquiring into its educational activities. In hospitals used for teaching purposes, it has been found that the clinical and scientific work is much improved, and such a hospital is an

TABLE II

	UPPER RESPIRATORY INFECTIONS	PNEUMONIA	TYPHOID FEVER	EPIDEMIC CEREBROSPINAL MENINGITIS	ERYSIPELAS	IMPETIGO	SCABIES	PEDICULOSIS	SYPHILIS	GONORRHEAL VAGINITIS	GENERAL OPHTHALMIC	ORTHOPEDIC	OTOLARYNGOLOGIC	NEUROLOGIC
General Wards	7	5	1	0	0	1	4	7	18	0	0	18	23	29
Infectious Precautions	5	3	0	1	1	5	8	11		0	0			1
Cubicles	22	25	5	5	6	6	5	6	2	2	2			
Isolation			19	16	21	17	9	5	11	13	18	16	10	3
Special Wards	0	1	2	3	3	3	3	3	1	5	3			
Not Admitted	0	0	7	9	3	2	2	2	1	14	9			
No Reply	1	1	1	1	1	1	1	1	2	1	1	1	1	1

In some instances it was impossible to tabulate one or more of the replies.

added asset to the community. Why hospitals in general have not seen this possibility and taken advantage of it is hard to account for.

Of the thirty-five children's hospitals, twenty-two are definitely associated with medical schools, and four loosely affiliated; consequently more than two-thirds of the children's hospitals in the country are used for teaching. Twenty-eight hospitals have clinics for medical students; twenty-seven have ward walks; and five have clinical scholarships.

For the practicing physician, nineteen hospitals offer clinics, and one other offers clinics by courtesy and special arrangement. These clinics vary greatly, the most frequent ones coming weekly (in six hospitals). Ward walks for practicing physicians are held in twenty-six of the hospitals. Postgraduate instruction is offered in nine, in three of which the number of students is not limited. The others vary from four to one hundred and fifty. The total number enrolled for 1932 for these postgraduate courses was in the neighborhood of two hundred and fifty. The courses varied between two two-day courses to a course covering one year.

The instruction of the internes is carefully attended to in most of these hospitals, in fact, clinical conferences are held in all but three hospitals. The number of these conferences varies very widely. In three hospitals there are daily conferences; in seven they are held once monthly; the most common interval seems to be once weekly which takes place in fifteen hospitals. We feel that clinical or pathologic conferences should be held at least once weekly in all hospitals. Pathologic conferences are held with internes in all the hospitals but seven, and these usually as often as once a week. Nineteen of the hospitals hold conferences in various specialties. Internes have special instruction in x-ray in nineteen hospitals, and in diagnosis and therapy in five. They receive special instruction in the pathologic laboratory in eight hospitals, in the bacteriologic laboratory in fourteen, and in the serologic laboratory in eight. They receive instruction in physiotherapy in only two of the hospitals, but they do receive instruction in diet and nutrition in seventeen. All but two of the hospitals have a medical library. This varies in size from twenty-five to thirty-one thousand volumes. All but four afford research facilities for the staff.

The educational facilities for the medical profession offered by the children's hospitals are distinctly above the average of those offered by other hospitals either special or general. There seems to be a realization that children's hospitals should be used for teaching, not only for the medical students, but to a large extent for postgraduates and for internes who are receiving their training in these hospitals. While conditions are not all that one could wish for, the relative position of the children's hospitals in the matter of medical education either to the student, internes, or practicing physician must be quite high.

e. Special Information

The routine custom of the staff in handling patients is quite varied. It is surprising that there is so much difference of opinion. That observation or isolation wards, which are certainly desirable, should not be found in all the hospitals is, of course, possibly due to a lack of space; but that throat cultures, vaginal smears, etc., are not routine measures, must be a surprise to anyone familiar with the work among children. There is a general agreement that when the child enters the hospital that blood counts, urinalyses, and tuberculin tests should be made, and a complete history and physical examination, of course, should be required in all hospitals.

The handling of special cases is best exemplified in Table II, which needs very little comment. The wide variation of opinion as to what should be done with certain cases, is shown best in Table II.

News and Notes

The **American Board of Pediatrics, Inc.**, met in St. Louis, Mo., January 13, and adopted by-laws and rules and regulations for certification. The following officers were elected: Borden S. Veeder, President; Henry L. Helmholz, Vice-President; C. Anderson Aldrich, 723 Elm Street, Winnetka, Ill., Secretary and Treasurer. The entire membership, which was announced in the December, 1933, issue of the Journal was present.

The following classification of groups for purposes of certification was decided upon.

Group 1

Physicians who have limited their practice to pediatrics for over ten (10) years.

Until September, 1936, suitable applicants may be certified on record although examination is optional with the Board. After September, 1936, all candidates for this group will be required to take an examination.

Group 2

Physicians who have limited their practice to pediatrics for from six (6) to ten (10) years.

Applicants must submit evidence of at least one year's hospital training and one year's training in a recognized pediatric center and of continued work in some form of pediatric organization or institution. Examination is required.

Group 3

Graduates of five (5) years or less. Applicants must submit evidence of having finished one of the following forms of training:

A. One (1) year's service in a general hospital with two (2) years' service in a pediatric center, or three (3) years' service in a pediatric center.

B. Two (2) years' service in a pediatric center plus two (2) years' specialized practice in pediatrics, including continued work in some pediatric activity.

C. One (1) year's service in a general hospital, one (1) year's service in a pediatric center plus three (3) years' service in the specialized practice of pediatrics including connection with some pediatric activity.

Examination is required on all applicants in this group.

The Board defines service in a pediatric center as full time devoted to rounded experience in an acceptable hospital, or a graduate course which includes ward and out-patient service including therapeutic and preventive pediatrics. The time served in pediatric centers need not be continuous or spent in the same institution.

The fee for certification was placed at $20.00. This is less than half of the fee charged by the other specialty examining boards and may have to be increased.

A booklet is being prepared containing details, and, as soon as it is published, will be sent to every member of the **American Pediatric Society** and the **American Academy of Pediatrics.** There is no continuing or membership list of the Section of Pediatrics of the A. M. A. Pediatricians not members of the two societies should apply to the Secretary for a copy.

It should be kept in mind that the **American Board of Pediatrics** is not a medical society. It was founded by action of the three national pediatric societies

mentioned above and is controlled by them as each appoints three members to the Board. The Board, therefore, is merely the agent of the three national societies and its sole function is to issue certificates of proficiency in pediatrics. There are no dues. The certification fee is to pay for the actual work of the Board. According to the articles of incorporation no member of the Board may receive any salary, bonus, or emolument of any kind.

On February 11, 1934, The Advisory Board on Medical Specialties was organized at a meeting in Chicago. The following organizations are included in the Board. Each organization appoints two members to this Board.

The American Board of Ophthalmology.
The American Board of Otolaryngology.
The American Board of Obstetrics and Gynecology.
The American Board of Dermatology and Syphilology.
The American Board of Pediatrics.
The Council on Medical Education and Hospitals of the A. M. A.
The Association of American Medical Colleges.
The National Board of Medical Examiners.
The Federation of State Medical Boards of the U. S. A.
The American Hospital Association.

Boards are in process of formation in radiology, orthopedic surgery, gastroenterology, proctology, and psychiatry.

Comments

IT HAS long been charged that mortality during pregnancy, labor, and the puerperium is high and unnecessarily high. Many studies of mortality statistics have been made, and little positive proof has been presented—at any rate proof acceptable to the profession at large. The basic facts on which these studies have been made are claimed to be inaccurate. The Report of the New York Academy of Medicine, prepared under the direction of Dr. Ransom S. Hooker, is the most careful and scientifically accurate collection of facts on this subject ever presented. After long study of the pitfalls and possible inaccuracies and with the advice of recognized statisticians, the assemblage and analysis of data of every maternal death occurring in New York City during the years 1930-1932 was undertaken.

During those three years 2,041 deaths occurred from conditions associated with childbirth. Data on each case were obtained within one month after death occurred by personal interview with the attendant concerned, and in hospital cases the bedside notes were also carefully studied. The facts were then assembled, and each month was studied by an advisory committee of four obstetricians of recognized ability and standing. The decisions were made without knowledge of who the attendant was in any case. It is well to emphasize the details, for the facts presented in the report are certainly startling. In the first place it demonstrated that studies of official death certificates do not give a true picture of the facts. There was an error in 17.8 per cent in stating the true cause of death. In 15.9 per cent of the cases no mention was made of the true cause of death, either as primary or contributory. This was particularly true of puerperal septicemia; in over 28 per cent of the cases this condition was never stated.

Of the 2,041 deaths 65.8 per cent were judged preventable. "That number of women, if they had had proper treatment and care, could and should have been brought safely through parturition." In only phlegmasia alba dolens and embolus and "accidents of puerperium" were the majority of deaths not preventable. And still more serious is the placing of the responsibility.

Of all these deaths judged preventable, in 61.1 per cent the responsibility was laid to the physician. In only abortion (nontherapeutic), albuminuria and eclampsia, and pernicious vomiting of pregnancy was the responsibility laid to the patient in the majority of cases. Of these preventable deaths laid to the physician, approximately half were due to errors of judgment and half to errors of technic.

Let it be remembered that these decisions were made by men of recognized ability and judgment, who were studying work in which they specialized. "Whenever there was doubt or disagreement, or where complete data on any cases were lacking, the judgment was 'not preventable.'" It is perhaps wise to mention the basis on which this preventability was judged. "In judging whether or not the death was inevitable, the criterion was that of the best possible skill both in diagnosis and treatment which the community could make available."

The most frequent cause of death was puerperal septicemia, 25 per cent of all deaths! And this exclusive of abortion and ectopic gestation. It was almost five times as high following operative delivery as in spontaneous delivery. Of the preventable cases, 75 per cent of the total, almost 82 per cent were ascribed to errors

on the part of the physician, errors of technic being almost twice as many as errors of judgment. The report states that the "reproach" to obstetrics that the incidence of puerperal septicemia has not materially lessened in these days of asepsis, as it has in surgery, is only partly deserved. The lower genital tract is always a potentially infected area, but the organisms there present are usually nonpathogenic until conditions are changed when they may become very virulent. These conditions are generally believed to be due to lowered resistance of the tissues from severe hemorrhage, shock, and tearing or bruising of the soft parts. In other words, poor obstetric technic. "The avoidance of this type of infection, therefore, depends on good obstetric judgment and on the skillful performance of obstetric operations when they are indicated."

But the majority of the septicemia cases comes from hemolytic streptococci introduced by droplet infection of the hands and instruments by attendants who are carriers of these organisms. Infection from septic lesions on the hands or person of attendants is considered unusual. The type of infection in puerperal septicemia has therefore changed since the days of Semmelweis and Oliver Wendell Holmes, but the infection still occurs.

Hemorrhage was directly responsible for nearly 10 per cent of all the deaths, and of these over three-quarters were considered preventable. Of the preventable deaths, the physician was held responsible for over three-quarters, in this case errors of judgment being almost twice as frequent as errors of technic.

Accidents of labor, the cause of over 8 per cent of the deaths, were preventable in 87 per cent of the cases, and the physician was held responsible in almost 90 per cent of them—his errors being about equally those of judgment and of technic.

Among the causes of deaths in which the patient herself was considered responsible more often than the attendant, the most frequent cause was albuminuria and eclampsia—over 11 per cent of all deaths—and here the blame was laid to the woman in 69 per cent of the preventable cases. "The studies of these cases revealed a surprising tendency to disregard manifest danger signals, very many of the women being first brought under observation at the time of the first convulsion."

To do more than touch the high points of this report is impossible. Every one of its 222 pages and 50 more pages in the Appendix is worthy of careful study by every obstetrician and every physician who takes obstetric cases, nay, by every physician. The report emphasizes in much detail, the lack of suitable prenatal care, due to the ignorance of the laity of its necessity and too often the insufficient care given by the physician when it is sought. It states with utter frankness where the responsibility seemed clearly to lie for maternal deaths. Proper care was not given, according to the report, in 65 per cent of the cases, but "where the lack of proper care was ascribed to failure on the part of the attendant, it is probable that the failure was not attributable to neglect or carelessness. Rather, the ignorance and insufficient training of the attendant prevented him from giving the high quality of care which he was attemptig to provide for his patient, and, further, prevented the understanding on his part of the fact that he was incapable."

That is the real crux of the situation, and we are back again to the frequent criticism that medical education is failing to teach the fundamentals in obstetrics, as well as in many other branches of medicine. The medical schools must give sufficient training in normal obstetrics, but they must do more. They must "inform the student that the training which he receives does not qualify him to practice as a specialist in obstetrics. His training is to enable him to conduct normal labors and to be able to recognize and evaluate the abnormalities requiring the services

of a specially qualified obstetrician. The medical profession *must* insist that prolonged graduate study is necessary for specialization." Such opportunities must be made available and must be adequate.

The medical profession is equally obligated to teach the lay public what safe obstetrics is; that adequate prenatal examination and continued observation is essential; that the patient must be informed of the possible gravity of symptoms which may seem to her unimportant; that "operative delivery, undertaken merely to alleviate pain or shorten labor involves increased risk to both mother and baby."

The report also emphasizes that four walls, a roof, an operating room and a score or more of beds do not constitute a hospital. If honestly studied, its findings of hospital deaths point to the increased danger inherent in crowding together a number of patients unless the utmost care and attention is given to securing the most complete asepsis possible. It states that these conditions do not exist in a great number of the hospitals, especially the so-called proprietary hospitals.

This report is the result of work done at the express desire of a large body of obstetricians. That it should be criticized by the incompetent is not strange. But what will the obstetricians as a whole do about it? It is the strongest argument yet produced for the necessity of certifying "specialists" and should be of the greatest assistance to the efforts of the American Board of Obstetrics and Gynecology. It is an honest, fearless, conservative statement of the results of a remarkable personal study of every death associated with childbirth in a community of six million people over a period of three years. It is worth careful study.

Erratum

In Dr. Sweet's review of "The Diagnosis and Treatment of Postural Defects" by Phelps and Kiphuth, in the December, 1933, issue of the Journal, p. 943, the sentence beginning on line 17 should read:

"A moccasin is, I am certain, the only form of shoe for normal infants until the full development of skillful coordinated walking which does *not* interfere with the best development of the muscular power and functional skill of the feet."

The Journal of Pediatrics

CONTENTS FOR MARCH, 1934

Original Communications

Obesity in Children. Norman K. Nixon, M.D., Los Angeles, Calif. ---------- 295

Nonspecific Infectious Granuloma and Carcinoid of the Appendix. Jay Ireland, M.D., Chicago, Ill. ---------- 307

Insulin in Undernourished Nondiabetic Children. Leo S. Radwin, M.D., and Samuel S. Brown, M.D., Brooklyn, N. Y. ---------- 315

Fatigue in School Children. Charles G. Kerley, M.D., New York, N. Y. ---------- 322

The Use of Oxygen in the Care of Feeble Premature Babies. William P. Buffum, M.D., and George F. Conde, M.D., Providence, R. I. ---------- 326

The Serum Treatment of Pneumonia in Children. Camille Kereszturi, M.D., and David Hauptmann, M.D., New York, N. Y. ---------- 331

Calcinosis Universalis and Dermatomyositis. Councill C. Rudolph, M.D., St. Petersburg, Fla. ---------- 342

Achondroplasia in a Twin. Edward L. Benjamin, M.D., and Abraham Brookner, M.D., New York, N. Y. ---------- 352

The Effect of Small Quantities of Breast Milk, Liver Extract, Iron and Copper, Respectively and in Combinations, Upon the Iron Balance of Artificially Fed Infants. Siegfried Maurer, M.D., Joseph Greengard, M.D., W. L. Curtis, S.B., and Cessa Klüver, S.B., Chicago, Ill. ---------- 356

Constipation in Breast-Fed Infants Caused by Anorectal Fissure. Don F. Cathcart, M.D., Atlanta, Georgia ---------- 366

Renal Rickets, George B. Bader, M.D., New York, N. Y. ---------- 368

Report of Three Cases of Congenital Heart-Block With a Résumé of the Literature to Date. Luvern Hays, M.D., Ann Arbor, Mich. ---------- 380

Lymphangiectasis With Chylorrhea. Henry G. Poncher, M.D., and Thomas P. Saltiel, M.D., Chicago, Ill. ---------- 387

The Diagnostic Tuberculin Reaction. Joseph Greengard, M.D., and Samuel J. Nichamin, M.D., Chicago, Ill. ---------- 393

Brucella Infection in Children. Angus McBryde, M.D., N. C. Daniel, M.D., and M. A. Poston, Durham, N. C. ---------- 401

Pediatric Clinics

The Babies Hospital and Department of Diseases of Children, Columbia University, New York. Rustin McIntosh, M.D., New York, N. Y. ---------- 406

Critical Review

Allergic Diseases, Francis Scott Smyth, M.D., San Francisco, Calif. ---------- 410

American Academy of Pediatrics

Proceedings—Report of the Committee on Hospitals and Dispensaries ---------- 418

News and Notes

News and Notes ---------- 426

Comments

Comments ---------- 428

Pioneers in Malt Therapy
Since 1875

In 1875 the world was startled by news of the discovery of gold in Deadwood and Whitewood gulches, right in the heart of the Black Hills of Dakota. In that same year The Maltine Company began pioneering in the field of malt therapy and, paralleling the news of the discovery of gold, announced to the medical profession its first product—Maltine With Cod Liver Oil.

While The Maltine Company admits a just pride in its 59-year-old record of achievement, past successes but spur the company to greater aggressiveness in the search for betterment. New products, bearing the honored name "Maltine," which have been introduced from time to time, attest the alertness and untiring zeal of the Maltine Laboratories in their endeavors to improve and further develop worthy products.

1875: *Gold discovered in Deadwood Gulch*

Maltine With Cod Liver Oil is perhaps the best known and most widely used of the Maltine products. Constant supervision and testing maintain its high quality. It is composed of 70% Maltine, a concentrated fluid extract of the nourishing elements of malted barley, wheat and oats—excellent sources of vitamins B and G—and the 30% balance of vitamin-tested cod liver oil of high potency in vitamins A and D. When administered with either tomato or orange juice, vitamin C is added, thus providing five vitamins.

Maltine With Cod Liver Oil is biologically standardized and *guaranteed* to contain vitamins A, B, D and G. Biological report will be sent to physicians and institutions on request. Address The Maltine Company, 30 Vesey St., New York, N. Y.

This Trade-mark Identifies the Only Genuine

Maltine

Reg. U. S. Pat. Off.

WITH COD LIVER OIL—Introduced in 1875

Member NRA
We do our part